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Abstracts of papers presented for the annual meeting scheduled for Cleveland, April 6–10, 1943. On account of the cancellation of this meeting, all the papers are to be regarded as "read by title." For possible correction in any of the abstracts see the next issue.

The effect of bile salts on the excretion of cinchophen and neoarsphenamine. J. H. ANNEGERS (by invitation), F. E. SNAPP (by invitation) and A. C. IVY. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* The excretion of cinchophen and of neoarsphenamine was studied in 12 bile fistula dogs. The drugs were given in doses of therapeutic proportion on a body weight basis. After the biliary excretion of the drugs was determined with no return of bile or administration of bile salts, the tests were repeated giving three grams of oxidized, unconjugated or of unoxidized, conjugated bile salts daily.

The excretion of neoarsphenamine was not increased significantly with either bile salt preparation. An average of 27.2 per cent of intravenous doses of neoarsphenamine was excreted in bile when no bile salts were given. An average of 29.0 per cent and of 22.0 per cent occurred with the administration of conjugated unoxidized and with oxidized unconjugated bile salts, respectively.

The excretion of cinchophen was facilitated by the administration of either bile salt preparation. An average increase in cinchophen recovery of 18 per cent occurred when conjugated, unoxidized bile salts were given, and of 16 per cent when oxidized, unconjugated bile salts were given. [*This work was assisted in part by a grant from the Dawes-Atkinson Fund of Northwestern University.*]

The retention of atabrine in the animal body, its excretion in bile and urine, and its effect on cholic acid output. J. H. ANNEGERS (by invitation), F. E. SNAPP (by invitation), A. C. IVY and A. J. ATKINSON. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* Atabrine was given subcutaneously in doses of 5.0 mgm. daily for five days to 24 white rats. Each rat was killed and the entire carcass extracted for atabrine. Twenty-four hours after the last dose, 29.5 per cent remained in the tissues. There was a progressive decrease, and the tissues were nearly free of the drug in three weeks, and completely free in five weeks.

Five dogs were given 150 mgm. of atabrine orally in divided doses daily for one week. Twenty-four hours after the last dose, 6.0 per cent of the drug was recovered from the liver. On the 3rd, 10th, 17th, and 52nd days after stopping the drug, 4.8, 1.4, 2.2, and 0.51 per cent, respectively, was recovered from the liver.

Biliary excretion of atabrine was studied in six bile fistula dogs after oral doses of 150 mg. daily for one to six days. After 24 hours, an average of 4.8 per cent of oral doses was recovered from the bile when no bile was returned, and 8.0 per cent was recovered when bile was returned every 8 hours; 24 hour urinary excretion was 4.0 per cent when no bile was returned; and 5.2 per cent when bile was returned to the intestine every eight hours. Total 24 hour atabrine recovery in bile and urine was 9.7 per cent of oral doses when no bile was returned and 11.5 per cent when bile was returned every 8 hours.

Simultaneously cholic acid output was studied. No significant change in cholic acid output occurred.

Further investigations on the insulin sensitivity of the hypophysectomized-adrenodemedullated rat and on the rôle of the adrenal cortex. V. ARNETT (by invitation) and E. GELLHORN. *Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.* In order to evaluate the rôle of the adrenal cortex in insulin sensitivity, the effects of fasting and insulin were studied in hypophysectomized-adrenodemedullated (h-a) and hypophysectomized-adrenalectomized (h-adr) rats. In contradistinction to our earlier work the h-a rats were first demedullated and ten days later hypophysectomized. They were used for the insulin test (0.01 u/kgm) 2–5 days later. It was found that nine sensitive h-a rats showed an average blood sugar of 93 ± 4.4 mgm. per cent after 6 hours fasting whereas ten h-adr rats were already in a hypoglycemic state (blood sugar 77 ± 11.5 mgm. per cent determined after Hoffman). The hypoglycemia made this group less suitable for the insulin test than the h-a group. The experiments indicate that the adrenal cortex delays the fall of blood sugar on fasting in spite of its gradually developing atrophy. One hour after injection of insulin the blood sugar of the h-a rats averaged 60 ± 6.3 mgm. per cent whereas it was 83 mgm. per cent after 8 hours fasting without insulin. In two h-a's the adrenal cortex seemed to be still functioning 14 and 28 days after hypophysectomy judging from fasting blood sugar and insulin sensitivity. The experiments confirm the work of Gellhorn, Feldman, and Allen and present evidence for the functioning of the adrenal cortex in spite of progressive atrophy. [*Aided by a grant from the Josiah Macy Foundation.*]

The relation of the diet to the composition of tissue phospholipids. CAMILLO ARTOM and WIL-

LIAM H. FISHMAN (introduced by Arthur Grollman). *Dept. of Biochemistry, Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, N. C.* Male albino rats raised to about 100 grams on a mixed stock diet (containing 25 per cent proteins) were transferred to a synthetic casein diet (10 per cent casein, technical, 5 per cent cod liver oil, 5 per cent Crisco, 75 per cent carbohydrates, plus minerals and yeast extract). Analyses were made for total lipids, choline and non-choline containing phospholipids, sphingomyelins, non-phospholipid fatty acids, and unsaponifiable matter in the liver and skeletal muscles.

A considerable decrease in the choline containing phospholipids (calculated per 1 gram of delipidized liver) was observed, the maximum decrease of about 50 per cent occurring on the 12th day. A slight but definite tendency toward higher values was apparent in the subsequent period. Non-choline containing phospholipids were affected to a lesser degree. Similar results were obtained with diets containing 5 or 30 per cent casein, except that with the 30 per cent diet the decrease was less considerable and the tendency toward the recovery more marked.

In the two months old rats, supplementation of the casein diet with choline HCl, choline + cystine, serine, ethanolamine, or glycine, was quite ineffective in preventing or correcting the changes in the liver phospholipids. Supplementation with cystine or methionine caused an increase in both the weight of the delipidized tissue and in the total amounts of phospholipids in the total liver, but the concentration per gram of delipidized tissue remained unaltered.

Recently weaned rats on the 10 per cent casein diet showed also a decrease in the concentration of lecithins when compared with similar rats on the adequate stock diet. But, unlike other more mature rats, the decrease is prevented by the daily administration of choline.

Intracellular water changes in Rhesus monkeys, and rats in profound cold hypothermia without drugs. H. G. BARBOUR, ELIZABETH A. MCKAY (by invitation) and W. P. GRIFFITH (by invitation). *Dept. of Pharmacology, Yale Univ. School of Medicine, New Haven, Conn.* Monkeys in a 3°C room for one hour lost about 3.5°C in body temperature; serum proteins (from specific gravity) and chlorides (Van Slyke and Sendroy) rose about 3 per cent agreeing with previous work here.

Monkeys chilled in the same room by applying to the ventral surface a half-inch copper coil with water circulating at 7°C, lost hourly 5.5°C; serum proteins rose 1 to 6 per cent (maximum at body temperature 35°C). Chlorides (usually after some fall) rose to a maximum at about 30°C body temperature. At 20°C the average chloride level was 2.4 per cent below normal.

It is concluded that ordinary exposure of monkeys to cold, with retention of reflexes, leads to a gain of intracellular water (as in cats, Barbour, Am. J. Physiol. 129: 304, 1940). When however, the hypothalmus becomes so chilled (without an anesthetic) as to abolish reflex responses to cold, water tends to leave the cells.

Monkeys rewarmed from 20°C to normal exhibit very slow recovery of water by the cells.

Serum and tissue chloride studies in groups of 5 or more rats killed after similar treatment confirmed the above, except that there was less evidence that the level of intracellular water in chilled rats became subnormal. Rats in the 3°C room (with metabolic rate +40) gained intracellular water in muscle and liver respectively 3.9 per cent and 14.7 per cent, while in rats chilled (with metabolism −40) to about 20°C by cold coils, intracellular water of muscle was 0.5 per cent below normal, while that of the liver was still 11.9 per cent above normal.

Residual effects of oxygen at high barometric pressure. JOHN W. BEAN and ERNEST C. SIEGFRIED (by invitation). *Dept. of Physiology, Univ. of Michigan.* It has been frequently stated that the action of oxygen at high barometric pressures (OHBP) is entirely reversible and that recovery is immediate and complete on decompression. There is however some indication of residual effects. In an attempt to investigate such effects, albino rats were exposed to oxygen at pressures of from 5 to 6 atmospheres for periods of from 15 to 20 minutes duration. Single exposures, and two or three exposures a day for several successive days were used. Decompression such as to prevent O_2 bubble formation was begun at the onset of convulsive seizures, or when there was evidence of disturbed neuromuscular coordination in any one of the group of animals exposed.

It was found that even after one exposure some animals which experienced a distinct convulsive attack retained very pronounced hypertonic motor paralyses, with a predilection for the forelimbs. The persistence of the dysfunction was more prolonged after severe convulsive attacks and in some cases appeared to be permanent. The occurrence of the convulsive seizure is not essential however to the induction of this residual loss of function for it was found in animals which experienced no convulsive attacks but which were subjected to several successive exposures to OHBP. The results demonstrate that exposure to OHBP, particularly where successive exposures are involved, induce alterations which are not completely reversible, at least for periods as long as ten weeks. It is suggested that this incomplete reversibility is due to an irreversible change in enzymatic cellular processes (Bohr, D. F. and J. W. Bean. Am. J. Physiol. 131: 388, 1940) particularly within the C.N.S.

Permeability to water in Pelomyxa carolinensis. W. H. BELDA (introduced by S. O. Mast). *The Johns Hopkins Univ. and the Marine Biological Lab.* Specimens of a multinucleate amoeboid organism, Pelomyxa carolinensis (Wilson), were transferred from culture fluid of known concentration to 0.1 M. and 0.2 M. solutions of mannitol erythritol, and lactose. The specimens were measured at the time of transfer and at intervals of 1, 2, 4, 6, 12 and 24 hours after transfer. The specimens decreased in volume in these solutions, at first rapidly, and then more slowly. The decrease was greater in 0.2 M. solutions than in 0.1 M. solutions.

Other specimens were transferred from culture fluid to distilled water and measured as above. During the first two hours they increased in volume, and then very slowly decreased.

Specimens kept in culture fluid eliminated water through the contractile vacuoles equal to 3.8 per cent of the total volume of the organism per hour; in specimens kept in distilled water the rate was 6.4 per cent; in specimens transferred to the hypertonic solutions named above the output of the contractile vacuoles dropped rapidly, approaching zero after 80 minutes.

From the gain or loss of water ascertained by measurements of the change in volume, with corrections for water eliminated through the contractile vacuoles, the rate of permeability was calculated. During the first hour of shrinking in hypertonic solutions, the average rate of permeability was 0.031 cubic micra of water per square micron of cell surface per minute per atmosphere. After one hour the rate decreased. During swelling in distilled water the rate of permeability did not vary with time; the average value was 0.022.

The return of electrical activity in regenerating nerve fibres. C. M. BERRY (by invitation), H. GRUNDFEST and J. C. HINSEY. *Dept. of Anatomy, Cornell Univ. College of Medicine, New York City and Dept. of the Laboratories of the Rockefeller Inst. for Medical Research, New York City.* A combined study of the electrical and histological properties of regenerating nerves was made on 51 cats. The right tibial, peroneal and saphenous nerves were divided, sutured and allowed to regenerate for 2 to 45 weeks. The nerves were first stimulated in situ to observe the return of motor and sensory function, then excised and placed in a moist chamber at 38 degrees C for examination of their electrical activity. They were fixed later for histological study.

The first electrical responses were observed at 2 weeks and were slowly conducted. (1 to 2 mps.) The maximum velocity of conduction then increased with post-operative time and after 45 weeks reached about 80 mps. in peroneal and tibial nerves. The diameters of the largest regenerating fibers increased similarly. The relation between the diameters and the conduction velocities of the regenerating fibers was approximately linear like that found in nerves of normal growing and adult cats.

As impulses traveling in the large fibers central to the suture passed into their smaller peripheral outgrowths, their velocities decreased abruptly. The fibers conducting most rapidly below the suture had central rates of 30 to 120 mps. Therefore, the largest peripheral outgrowths did not always come from the largest axons.

The rates of regeneration were similar to those found by others. (J. Z. Young, Physiol. Rev. 22: 318, 1942.) Regenerating fibers showed higher threshholds to stimuli. They were responsive to repetitive stimuli.

The excretion of sympathomimetic amines (tyramine and paredrine) by man. KARL H. BEYER and J. W. STUTZMAN (by invitation). *The Dept. of Physiology, Univ. of Wisconsin Medical School, Madison.* Because tyramine (p-hydroxyphenethylamine) is rapidly deaminated *in vitro* by aminase of liver and since both it and paredrine (p-hydroxyphenisopropylamine) are rapidly oxidized by phenolase from potatoes it has been supposed that these related compounds were destroyed in the body.

By an extraction—purification process tyramine and paredrine were removed from urine, coupled with a diazonium compound and identified by the resulting colored solution. Thirty milligram doses orally of either amine were excreted in considerable quantities within 2 hours and for a duration of at least 12 hours.

Experiments using the Warburg apparatus were performed which revealed that compared to control urine, excreted before the ingestion of 30 mgms. of either amine, urine collected within 8 hours thereafter showed a significantly greater oxygen uptake in the presence of phenolase, demonstrating the presence of the unconjugated phenolic portion of the molecule in urine. Also, sufficient quantities of the pressor amines were extracted from urine following their ingestion to give a significant rise in blood pressure when injected intravenously into anesthetized dogs.

It is proposed that since these compounds are only very slightly active orally in doses up to 50 mgm. they are quickly conjugated on being absorbed into the body, in which form they are refractory to the action of aminase and physiologically inactive. Carried to the kidneys the active compound is split from the inactive form either in the kidney parenchyma or in the urine as it passes through the urinary tract.

An analysis of the rôle of magnesium sulphate in evacuation of the biliary tract. E. A. BOYDEN, GEORGE S. BERGH (by invitation) and JOHN

A. LAYNE (by invitation). *Depts. of Anatomy, Surgery and Medicine, Univ. of Minnesota.* Data obtained from 10 series of cholecystograms of students and from manometer readings of 12 choledochostomized patients demonstrate that while $MgSo_4$ acts with less force than egg-yolk—gall bladder volume being reduced in 30 minutes by only 42 per cent (cf. 71 per cent after egg-yolk) and sphincter resistance being lowered only 3.1 cm. (cf. 7 cm. after egg-yolk)—nevertheless it acts for the same time and in the same way as egg-yolk. Thus, after each substance was administered, gall bladder contraction ceased approximately 33 minutes later (av. for each group of 9–12 students) and sphincter resistance reached its lowest point approximately 22 minutes later (av. for each group of 9–14 patients). This suggests that $MgSo_4$ is not local in its action, but that like egg-yolk it gives rise to a hormone that is transmitted to both gall bladder and sphincter. That it induces less reaction in each organ than egg-yolk may be due to the fact that it is not absorbed as readily, or that it is not chemically so effective. The other observation—that duration of fall in resistance of sphincter is less than duration of contraction of gall bladder, in response to ingestion of either substance—may be explained on the basis that the hormone must overcome a tonic contraction of the sphincter which, there is some evidence for believing, is maintained by a local nerve net (Johnson and Boyden. Surg. Gynec. and Obstet., 1943).

Hemorrhagic and anoxemic anoxia in shock. BERNARD L. BROFMAN (by invitation) and HAROLD D. GREEN. *Dept. of Physiology, Western Reserve Univ. School of Medicine, Cleveland, O.* Hemorrhagic anoxia was produced in 13 anesthetized dogs by progressive bleeding until the mean blood pressure fell to 40 to 50 mm. Hg. After 2–4 hours, during which approximately 25 per cent of the blood was reinjected to prevent further decline, reinfusion of the remaining blood resulted in a temporary rise in blood pressure followed by a gradual decline, death ensuing in 2 to 6 hours. Oxygen consumption was reduced 30 to 50 per cent during both hemorrhagic and the terminal hypotension.

Anoxemic anoxia was produced in 15 dogs by reducing the oxygen in the inspired air to 8–10 per cent for 2 to 5 hours. An initial rise in blood pressure was followed by a gradual decline which in some animals reached a critical level (50–70 mm. Hg) characterized by slowing, then cessation of respiration, cardiac slowing, rapid decline of blood pressure and death, unless air and artificial respiration were administered. Some dogs maintained an adequate blood pressure, in others the critical level was avoided by increasing the oxygen by 1–4 per cent. Rectal temperature remaining unchanged, oxygen consumption was constant during the anoxemia despite the increased cardiac activity and the 2–5-fold increase of respiratory minute volume. However, oxygen consumption decreased materially during the decline of arterial pressure. Upon return to air, blood pressure rose, but in 13 dogs it subsequently declined and the animals died in 3–12 hours.

Thirteen of 14 control dogs maintained a normal blood pressure for 10 to 16 hours when they were sacrificed.

Injury and action potential in relation to negative phosphate ions. W. E. BURGE and W. E. PUGH (by invitation). *Dept. of Physiology, Univ. of Illinois, Urbana.* The gastrocnemius muscle of a frog was removed and cut transversely near one end. When the cut end was placed against one non-polarizable electrode and the sound surface against another with a galvanometer in the circuit, a current of 0.275 microamperes passed from the positive sound surface to the negative injured end.

Application of 0.6 N $CaCl_2$ to the injured end, thus precipitating the phosphate, decreased the current practically to zero in 18 minutes, while a subsequent application of 0.6 N H_3PO_4 to the injured end of this same muscle restored the current almost to its original strength in 18 minutes.

Application of 0.6 N $MgCl_2$ to the injured end of a muscle decreased its negative potential only about one tenth as much as did 0.6 N $CaCl_2$ in 18 minutes in keeping with the fact that magnesium is only about one tenth as effective as calcium in precipitating phosphate.

Application of 0.6 N NaCl had little or no effect on the negative potential of the injured end of a muscle in 18 minutes in keeping with the fact that NaCl does not precipitate phosphate.

These observations suggest that injury potential may be due to negative phosphate ions. Close similarity of stimulated and injured muscle suggests that the negative potential of contracted muscle like that of injured may be due to negative phosphate ions, ionizable inorganic phosphate being formed in both. Stimulated muscle may be regarded as slightly injured muscle, for any agent which will stimulate will injure if of sufficient intensity.

Nerve impulse in relation to free phosphate ions. W. E. BURGE. *Dept. of Physiology, Univ. of Illinois, Urbana.* The gastrocnemius muscle of a frog was removed with a long piece of its nerve attached. The nerve was blocked near the muscle with novocain. One non-polarizable electrode was placed on the nerve near the block and another at a distance from the block with a potentiometer in the circuit. Stimulation of the nerve near its end, with moderately strong tetanic shocks, set up negative charges which passed along the nerve, accumulated near the block and rendered this area

of the nerve temporarily electronegative. Stimulation of the nerve for ten seconds increased the negative potential of the area of the nerve near the block −25 microvolts × K over that of a portion of the nerve further away from the block.

Attempts were made to analyze these two portions of the frog's nerve for free phosphate according to the method of Youngburg, but the material was too small in amount for analyses. So the vagi nerves of large dogs were blocked, stimulated and the portions of the nerve near the block where the rise in negative potential occurred as well as similar portions further away from the block were analyzed for free phosphate ions.

It was found, in the ten dogs used, that the portions of the nerve near the block where the rise in negative potential occurred contained 11 per cent more free phosphate than the portions of the nerve further away from the block.

These observations suggest that nerve impulses are propagated pulses or surges of ionization of phosphate.

Muscular exercise, fatigue, and exhaustion in relation to brain potential. W. E. Burge. *Dept. of Physiology, Univ. of Illinois, Urbana.* When one electrode was placed on the forehead as near over the motor area as the receding of the hair would permit and another on the forearm, with a galvanometer in the circuit, a current passed from the forehead to the forearm, thus showing the forehead to be electropositive. The strength of this current varied with the activity of the subject.

During rest the current decreased practically to zero. During three minutes of wrestling, it increased to 1.25 microamperes; during the next three minute bout to 2.75 microamperes; during the next bout when the wrestlers had begun to fatigue, instead of increasing, the current decreased to 1.75 microamperes; and during the final bout when the wrestlers were exhausted, the current decreased to zero and reversed its direction to the extent of −0.75 microamperes. This reversal could be produced at the beginning of the wrestling season, but not later in the season when the men were in training.

We had found that the positive potential of the scalp fluctuated with the negative potential of the underlying cortex so scalp potential can be used as an index to cortical potential. Hence the rise in positive potential of the scalp during exercise (wrestling) indicates an increase in the negative potential of the underlying motor cortex, and the fall in scalp potential in fatigue indicates a decrease in negative potential of the underlying motor cortex brought on by excessive loss of negative charges or nerve impulses passing out over motor nerves to the muscles.

The effect of maternal thyro-parathyroid deficiency on fetal thymic size. D. Bailey Calvin. *Dept. of Biological Chemistry, Medical Branch, Univ. of Texas, Galveston.* In previous reports it was pointed out that thyroid deficiency in the mother during the period of gestation led to increased thymic gland size in the new-born white rat fetus. Hypothyroidism was induced in the female by partial or complete thyro-parathyroidectomy. The first data presented were obtained from litters delivered by operated females receiving only calcium gluconate or lactate supplements in the diet and drinking water Many females were unable to survive gestation or parturition, due to the hypo-parathyroid condition following operation, and died in hypocalcemic convulsions. Blood calcium values were considerably below normal.

Another series was carried through in the same manner, except for the use of small dosages (0.1–0.15 ml. per day) of parathyroid extract (Lilly). The maternal fatalities were decreased to a low percent and breeding, impregnation, gestation and parturition were far more satisfactory. Blood calcium levels were low normal.

In a third series of animals, even more parathyroid extract was used (0.25–0.50 cc/day), other conditions being the same. Further improvements in the females were noted.

For the three groups studied fetal thymic weights decreased toward normal as the well being of the mothers improved as a result of parathyroid therapy. In the third group the average fetal thymic weight was approximately 10 per cent above normal as compared to values of 20–25 per cent for group two, and 20–50 per cent in fetuses from operated mothers given only calcium salt supplements to compensate for the hypo-parathyroid condition.

It would seem, therefore, that, although thyroid efficiency in the mother may have some effect on fetal thymic size, the greater effect may be attributed to parathyroid deficiency and its attendant hypocalcemia.

The effect of p-aminobenzene-sulfonamide and 2-sulfanilylaminothiazole upon the capacity of monkeys to withstand low atmospheric pressures. James B. Campbell (by invitation) and Ebbe C. Hoff. *Laby. of Physiology, Yale Univ. School of Medicine, New Haven, Conn.* Young, mature monkeys (*Macaca mulatta*) were subjected to simulated high altitudes by decompression at two different rates: In slow "flights", pressure was reduced to 400 mm. Hg in 10 minutes and subsequently diminished by 50 mm. Hg stages at 10-minute intervals. In fast "flights", animals were decompressed to 400 mm. Hg in 1 minute followed by 100 mm. Hg "ascents" with 5-minute intervals at each level. "Ceilings" attained in slow control runs varied between 250 and 180 mm. Hg (average, 220 mm. Hg), decompression lasting from 44 to 95

minutes from onset to point of apnea (average duration, 63 minutes). The average control "ceiling" at the fast rate was 241 mm. Hg (average duration, 20 minutes). After oral administration of 0.5 gms. of p-aminobenzene-sulfonamide (sulfanilamide), most animals showed greater tolerance to decompression at the slow rate, supporting runs as long as 97 minutes and reaching pressures as low as 180 mm. Hg. When sulfanilamide administration was followed within 2 to 5 hours by fast decompression, the "ceiling" was always lower than in previous slow or fast controls (250 to 290 mm. Hg).

Preliminary experiments suggest that 2-sulfanilylaminothiazole (sulfathiazole) diminishes the tolerance of monkeys to both fast and slow "flights." With one exception, muscular tremors and convulsive episodes commonly seen during control runs did not occur during decompression after sulfanilamide or sulfathiazole administration. Typical flattening of the T-waves of the electrocardiogram observed in control experiments was never present in fast "flights" after sulfanilamide medication.

Mechanism of fertilization of eggs. MATILDA MOLDENHAUER BROOKS. *Univ. of California, Berkeley.* The oxygen consumption of *Arbacia punctulata* eggs and larvae was measured by the Warburg method. Methylene blue and KCN (0.004 per cent and 5×10^{-4} M respectively) were used to change the rate of O_2 consumption. There is a direct relation between the rate and the redox potential of cells (Genevois, 1928; and Barron, 1930). Therefore changes in the rate by these reagents are here interpreted to mean changes in the redox potentials of the electromotively active enzyme systems controlling the rate.

The following conclusions are arrived at: the redox potential is low in unfertilized *Arbacia* eggs, rises at fertilization, is highest at gastrula and decreases again in the pluteus. Sperm has a high rate, therefore a relatively high redox potential. Sperm raises the redox potential of the systems when added to unfertilized *Arbacia* eggs, thereby producing fertilization. In such forms as *Cumingia*, the decreased rate on fertilization would be interpreted in the light of the above to mean that for these forms, the redox potential of the unfertilized egg is too high and would need to be lowered to the appropriate level to initiate cell division. From studies on artificial parthenogenesis, it appears that a specific substance is not necessary for the initiation of development. The suggestion is therefore offered that the process of fertilization is dependent directly or indirectly upon the establishment of the appropriate redox potential of the respiratory enzyme systems.

The determination of the median lethal dose (LD 50) of pentothal sodium [sodium ethyl (1-methyl-butyl) thiobarbiturate] for rats. EMMETT B. CARMICHAEL. *Dept. of Physiological Chemistry, School of Medicine, Univ. of Alabama, University.* The toxicity of pentothal sodium has been tested for both young and old rats. The drug was dissolved in water and the fresh solution was injected intraperitoneally Normal well fed animals were used: 1, 233 young rats (1 to 9 mo. old) and 2, 43 old rats (9 to 15 mo. old). The doses varied by increments of 5 mgm. from 100 to 140 mgm./kgm. for the young animals, and from 110 to 130 mgm./kgm. for the old animals.

The median lethal dose (LD 50) for young rats was about 125 mgm./kgm. and for old rats was about 120 mgm./kgm.

The Pasteur effect in bone marrow studied with carbon monoxide-oxygen mixtures. CHARLES E. CARTER (by invitation) and CHARLES O. WARREN. *Depts. of Anatomy and Physiology, Cornell Univ. Medical College, New York City.* Previous studies (C. O. Warren, J. Cell. and Compar. Physiol. 19: 193, 1942) have shown that at low oxygen tensions there is a reciprocal relationship between decrease in respiration and increase in glycolysis of rabbit bone marrow. This was interpreted as meaning that if a Pasteur enzyme is present in marrow, its affinity for oxygen is the same as that of the respiratory enzyme which is sensitive to reduced oxygen tension. The present experiments are an extension of this study in which marrow respiration was inhibited by CO rather than by low oxygen tensions. Suspensions of bone marrow cells were equilibrated with O_2-CO mixtures, the accuracy of which had been checked by oxygen analyses made by the dropping mercury electrode method. Respiration was measured manometrically, lactic acid formation chemically. Nine experiments were performed with gas mixtures ranging from 92 to 98 per cent CO. The average inhibition of respiration was 50 per cent as compared with a 45 per cent increase in glycolysis. Since 95 per cent CO in 5 per cent O_2 caused a 50 per cent decrease in respiration whereas with 95 per cent N_2-5 per cent O_2 there was only a 10 per cent decrease, the effects measured here are primarily direct effects of CO. The reciprocal relationship between decrease in respiration and increase in glycolysis in CO indicates that the enzyme systems responsible for these two effects have similar affinities not only for oxygen but also for CO. This throws doubt upon the existence in marrow of an independent Pasteur enzyme.

Glycogen content of various parts of the central nervous system of dogs and cats. ANNETTE CHESLER and HAROLD E. HIMWICH. *Dept. of Physiology and Pharmacology, Albany Medical College, Union Univ., Albany, N. Y.* Kerr determined the glycogen content of the cerebral cortex and obtained values for dogs, cats and

rabbits somewhat less than 0.1 per cent. Though cerebral glycogen was resistant to other influences it was reduced by hypoglycemia. In the present experiments the glycogen content of the various parts of the neuraxis was determined in newborn, 5–8 week old and adult dogs and cats. The glycogen content of the newest phyletic parts, the cerebral cortex and caudate nucleus of the cat and dog increased with age. For the intermediate portions, a moderate decrease was found in the thalamus and corpora quadrigemina of the cat, while in the dog the thalamus showed a slight rise and the colliculi no change. The percentage of glycogen of the oldest parts, the cerebellum, the medulla, and cord, fell progressively both in the cat and in the dog. Work is being continued to determine the effect of insulin on glycogen content of the various portions of the neuraxis. In preliminary experiments it has been observed that prolonged hypoglycemia reduces the glycogen content of all parts of the neuraxis of adult dogs and cats. [*Aided by a grant from the John and Mary R. Markle Foundation.*]

Effect of various forms of anoxia and of conditions causing excitation of sympathetic centers on leucocytosis. F. B. CLARE (by invitation), C. H. CRESS (by invitation) and E. GELLHORN. *Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.* The dependence of leucocytosis on the sympathetico-adrenal (s-a) system was investigated by using various procedures which centrally excite the s-a system. Normal, vagotomized (to exclude the vago-insulin system) and adreno-demedullated rats were used. No effect on the vago-insulin system was found but it was observed that electroshock and metrazol cause leucocytosis in normal and vagotomized rats and no change in adreno-demedullated rats. The maximal change averaged more than 100 per cent under these conditions. Typhoid-paratyphoid vaccine caused marked leucocytosis in normal and adreno-demedullated rats suggesting a direct action of the toxins on the bone marrow. The leucocytosis following electroshock, metrazol, and typhoid vaccine was neutrophilic.

Experiments involving various forms of anoxia (CO-poisoning, anemia following the removal of one-third of the total blood volume, and exposure of rats to a barometric pressure of 400 mm. for 12 hrs. daily) led to leucocytosis only in normal but never in adreno-demedullated rats. The experiments show that with the exception of typhoid-paratyphoid toxin procedures leading to s-a discharges cause leucocytosis. It is assumed that adrenalin acts on the bone marrow. [*Aided by a grant from the Josiah Macy Foundation.*]

Increased insensible water loss during exposure to low barometric pressure. W. D. COLLINGS (by invitation), H. G. SWANN, C. U. DERNEHL (by invitation) and J. K. CLINE (by invitation). *Depts. of Physiology and Preventive Medicine and Public Health, Univ. of Texas School of Medicine, Galveston.* Preliminary studies revealed that young adult rats exposed to a pressure of 380 mm. Hg lose 10 to 13 per cent of their body weight in 12 to 24 hours. Sea level controls under identical conditions (fasted, water *ad lib.*) lose about 8 per cent.

An analysis of this weight loss was made employing methods similar to those used by Hall (Biol. Bull. 42: 31, 1922). It was found that increased weight loss in test animals was due to an increase in insensible water loss unaccompanied by thirst. Urine volume was essentially identical in tests and controls.

That anoxia, and not reduced pressure *per se*, is the causative factor was established by allowing the test animals to breathe 99 per cent O_2 during exposure to a pressure of 380 or 190 mm. Hg. The increase in negative water balance did not occur. Furthermore, when anoxia was produced by giving rats a mixture of 10½ per cent O_2 and 89½ per cent N_2, at normal atmospheric pressure, the negative water balance was as great as that seen in air-breathing animals at 380 mm. Hg.

The likelihood that the observed phenomenon was caused by hyperventilation accompanying anoxia has been investigated, also. Rats were allowed to breathe mixtures containing 5, 10 or 15 per cent CO_2, 21 per cent O_2 and the remainder N_2. The insensible water loss showed no proportionality to the amount of CO_2 inhaled. However, the extent of water loss was almost as great as that seen in rats exposed to 380 mm. Hg in air.

Changes in angiotonin (hypertensin) and renin-activator (hypertensin precursor) in hemorrhage and shock. DEAN A. COLLINS and ANGIE S. HAMILTON (by invitation). *Dept. of Physiology, Temple Univ., School of Medicine, Philadelphia.* These experiments confirm our previous suggestion that dogs in hemorrhagic shock develop exhaustion of renin-activator.

Dogs were usually anesthetized with morphine and barbital. Using guinea-pig's ileum angiotonin was assayed in arterial plasma heated 6 minutes at 90°C. to destroy renin, renin-activator and hypertensinase. Before hemorrhage responses were minimal; after adequate hypotension increased responses invariably occurred. The active heat-stable material was probably angiotonin: samples from adrenalectomized dogs after hemorrhage also caused vasoconstrictor responses in the perfused rabbit's ear and elevations of blood pressure in intact dogs; increased responses never occurred with samples from nephrectomized-adrenalectomized dogs.

Renin-activator was determined by incubating plasma 6 minutes at 37°C. with an excess of renin

(kindly supplied in part by Dr. I. H. Page) before heating. Intact dogs showed diminution of renin-activator after prolonged hypotension (e.g., after consecutive periods of 95 and 80 minutes or more at 40–60 and 20–40 mm. Hg. respectively); angiotonin usually decreased following its earlier increase. Pronounced individual variations occurred. One animal showed extreme reduction of renin-activator after 60 minutes and another no reduction after 150 minutes at 40–60 mm. Hg. Preliminary destruction of hypertensinase did not alter the picture. Usually in adrenalectomized dogs angiotonin appeared less readily, and more prolonged hypotension was required to diminish renin-activator. Adrenalectomized-nephrectomized dogs in hemorrhagic shock showed marked increases in renin-activator.

Although assay on perfused rabbits' ears was less satisfactory, it corroborated these conclusions. [*Aided by a grant from the John and Mary R. Markle Foundation.*]

Effects on renal function of the onset of shock due to partially occluding limb tourniquets. A. C. Corcoran, Robert D. Taylor (by invitation) and Irvine H. Page. *Lilly Laby. for Clinical Research, Indianapolis City Hospital, Indianapolis, Ind.* Diodrast and inulin clearances, urine flow and blood hematocrit indices were observed under pentobarbital anesthesia during the onset of shock due to application of tourniquets which caused nearly complete cessation of arterial flow. The observations were made in normal dogs, in uninephrectomized dogs with single explanted kidneys and after bilateral renal denervation and splenectomy. As part of another study, beef metamyoglobin was given intravenously at the time of release of the tourniquets in two experiments.

During the slow limb swelling which follows application of the tourniquets, diodrast and inulin clearances and filtration fraction are usually greatly decreased, as is also urine volume. These values only slowly return towards normal with release of the constricting cords. The depression of renal function, unlike that which follows hemorrhage (Corcoran and Page, Fed. Proc., 1943) is not associated with corresponding changes in arterial pressure. Lasting impairment of renal function does not follow the procedure, nor do the values of diodrast and inulin clearances or TmD in conscious dogs differ significantly from those obtained under pentobarbital anesthesia. Prevention of local fluid loss by prior fitting of snug plaster casts in one dog minimized the changes of clearance, hematocrit and arterial pressure which followed application and release of the tourniquets.

The relation of the changes occurring in renal function to total renal plasma flow and renal extraction, the participation of renal nerves and the effect of erythremia (Taylor and Page, Fed. Proc., 1943) will be discussed from the observations made in explanted, denervated and splenectomized dogs.

Effects of hemorrhagic hypotension and of blood transfusion on renal function in dogs with normal and denervated kidneys. A. C. Corcoran and Irvine H. Page. *Lilly Laby. for Clinical Research, Indianapolis City Hospital, Indianapolis, Ind.* Diodrast and inulin clearances were measured during successive periods of hypotension (*ca* 60 mm. Hg, 60 min.) due to bleeding, and also during and after successive intra-arterial and intravenous transfusions of blood into anesthetized normal dogs, dogs with single explanted kidneys and after bilateral renal denervation. The changes observed were correlated with urine volume, arterial pressure, hematocrit index and plasma protein content. Renal extractions of diodrast and inulin were determined in the dogs with explanted kidneys and total renal plasma flow calculated.

With allowances for decreased extraction during hypotension and for excretion of "extra" diodrast during restoration of blood, diodrast clearance was shown to parallel renal plasma flow. Indirect evidence was obtained for addition of diodrast and inulin to renal venous blood, apparently from interstitial fluid. The interpretations of diodrast clearance and of filtration fraction in terms respectively of renal plasma flow and relative intraglomerular pressure are therefore altered in this abnormal state.

Transfusion restores renal blood flow and function and arterial pressure in normal dogs after an initial hypotension, but restitution of flow as well as arterial pressure is progressively less adequate with succeeding periods of hypotension, in part as the result of renal vasoconstriction. Dogs with denervated kidneys apparently maintain renal vasoconstriction after the initial hypotension and since they show slower recovery of function after restoration of pressure than normal dogs. The suggestion is made that high spinal anesthesia may prevent restoration of renal circulation in patients with crushing injuries in whom its restitution may be particularly important.

Thyroid and thyrotropic hormone in vertebrate animal sera. Savino A. D'Angelo (by invitation), Albert S. Gordon and Harry A. Charipper. *Dept. of Biology, Washington Square College of Arts and Science, New York Univ., New York City.* Blood sera from representative animals of several vertebrate classes were tested for their ability to further the metamorphic advance in young starved tadpoles (method of D'Angelo, Gordon and Charipper. Endocrinology 31: 217, 1942). Nine intraperitoneal injections of 0.05 cc. of the sera were administered, on alternate days,

to carefully selected groups of animals. Of the sera tested, those obtained from rats were the most effective, causing the most rapid growth of the hind limb. Cow serum was more effective than lamb and rabbit serum. The latter two possessed somewhat greater potency than horse serum. Sera from adult frogs, turtles, pigeons and hypophysectomized rats contained no metamorphosis-inducing capacity.

The thyroid glands of tadpoles injected with rat serum showed considerable activation (columnar epithelium, liquefaction and release of colloid). Very slight activation resulted from treatment with cow and rabbit sera whereas none was induced with lamb or horse serum. Frog, turtle, pigeon, and hypophysectomized rat sera were without effect on the histology of the tadpole thyroid.

It would thus appear that, for the sera tested, only that obtained from rats contained appreciable quantities of thyrotropic hormone. The effects of the other sera in accelerating metamorphosis are probably due to the presence of thyroid rather than thyrotropic principle.

The rôle of blood pressure in electroencephalographic changes during overventilation. CHESTER W. DARROW and JULIAN H. PATHMAN (by invitation). *Inst. for Juvenile Research, Chicago.* Hypocapnia of cerebral blood may be assumed to favor vasoconstriction. In the present study one minute periods of overventilation in sixty *unanesthetized human* subjects typically produce a marked fall in blood pressure. With adequate fall in pressure and no change in pulse rate, there may be no change in the electroencephalogram. If the fall (1) is lacking, (2) is not sufficient, or (3) does not persist throughout overventilation, increased alpha potential typically results. The increased alpha potential is apparently a concomitant of the cerebral vasoconstrictor tone.

If during overventilation fall in blood pressure there is an appreciable increase in pulse rate, there is typically also an increase in slow "delta" activity of the electroencephalogram. Hyperventilation slow waves in the electroencephalogram do not occur in our series without associated increase in pulse rate, except in a small group with pronounced sinus arrhythmia. Since hyperventilation increase in pulse rate occurs during fall in blood pressure and without either an associated effect on sympathetic palmar sweating or a decreased downward trend of blood pressure, increase in pulse rate is interpreted here as due to inhibition of parasympathetic tone. Electroencephalographic evidence of concomitant cerebral effects involving slow waves suggests that blocking of parasympathetic vasodilator impulses to the brain may render that structure susceptible to the spasmodic influence of hypocapnia.

Depression of experimental polycythemias by oxygen administration, soybean lecithin, and carbaminoyl-choline. JOHN EMERSON DAVIS. *Dept. of Physiology and Pharmacology, Univ. of Arkansas, Little Rock.* Experimental polycythemia was produced in 3 dogs by the daily administration of posterior pituitary solution according to our previously reported method (1942) and by cobalt feeding in 2 other dogs.

Pure oxygen was administered by closed inhalation method to 3 polycythemic dogs for one hour daily. In spite of continued daily injections of pituitrin, the red cell counts and hemoglobin percentages of these animals were gradually reduced by about 15 per cent during the 5 days on which oxygen was administered. Within 3 or 4 days following cessation of oxygen administration, the erythrocyte numbers of these dogs returned to their previous polycythemic values.

The daily oral administration of 3 grams of soybean lecithin to 3 dogs which had a "pituitrin polycythemia," and 2 dogs with cobalt-induced polycythemia, caused prompt reductions of 14 to 20 per cent in their red cell counts.

The administration of carbaminoyl choline chloride in a daily subcutaneous dose of 0.1 mgm. to four polycythemic dogs caused significant reductions of their erythrocyte numbers, despite continuation of the erythropoietic stimulating agents.

Total leukocyte counts did not vary significantly during the production or reduction of polycythemia. Two of the dogs had been splenectomized 6 months prior to these experiments and they responded in exactly the same manner as normal dogs.

Liver function and bile phosphatase in bile fistula dogs. VICTOR A. DRILL (by invitation), J. H. ANNEGERS (by invitation), F. E. SNAPP (by invitation) and A. C. IVY. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* The bromsulphalein retention (5 mgm./kgm. of body weight), serum phosphatase, and bile phosphatase were studied in 9 bile fistula dogs. The dogs received sufficient bile salts each day to maintain adequate bile flow. Abnormal liver functions developed in all dogs, as judged by bromsulphalein retention and serum phosphatase, within 1 to 12 days after operation. The serum phosphatase and bromsulphalein tests showed good correlation in detecting this damage. In three dogs the liver function tests returned to normal 8 to 13 days post-operatively, whereas the liver function of the other dogs did not improve even after 60 to 80 days of observation.

When the liver function tests were normal the bile generally contained between 5 to 30 units (Bodansky) of phosphatase per 100 cc. At the time abnormal liver functions developed the rise in serum phosphatase in 2 dogs was correlated

with a lowered excretion of bile phosphatase (1 to 12 units/100 cc.), whereas the increase of serum phosphatase in 7 dogs was associated with an increased excretion, or production (30 to 100 units/100 cc.), of bile phosphatase. As the period of abnormal liver function lengthened, 4 of the 7 dogs showed a fall of bile phosphatase to values below normal. The total output of bile phosphatase per 24 hours was between 10 to 45 units, while the liver function tests were normal. As the bile phosphatase (units/100 cc.) increased or declined, the total bile phosphatase per 24 hours showed a similar change from the normal range.

Comparative study of liver function tests in detecting hepatic damage produced by carbon tetrachloride. VICTOR A. DRILL (by invitation) and A. C. IVY. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* The following liver function tests were studied: bromsulphalein retention (5 mgm./kgm. body weight); serum phosphatase; intravenous galactose tolerance; prothrombin time; and serum bilirubin. Eight dogs were used, receiving 0.5 cc. of CCl_4 per kgm. of body weight twice a week by stomach tube. The bromsulphalein test became abnormal in all dogs after 2 or 3 doses of CCl_4. Only one dog showed an abnormal response to the intravenous galactose tolerance test at the time the above tests detected hepatic damage. Six of the dogs later developed an abnormal galactose tolerance curve as the doses of CCl_4 were continued, whereas one dog did not show any change from normal during the experiment. The prothrombin time did not become abnormal as early as did the bromsulphalein or serum phosphatase tests. The prothrombin time later increased in four of the dogs as the administration of CCl_4 was continued, whereas 4 dogs did not show any change from normal. Serum bilirubin, normally absent in the dog, was not detected during the experiment. Of the tests studied, bromsulphalein retention and serum phosphatase were most sensitive in detecting the type of hepatic damage produced.

Respiratory changes in pulmonary vascular capacity. CHARLES DUPEE (by invitation) and VICTOR JOHNSON. *Dept. of Physiology, Univ. of Chicago.* In motion picture studies in which the outputs of the right and left ventricles were estimated separately and simultaneously in dogs breathing normally, this laboratory has reported (Am. J. Physiol. 137: 620, 1942) that *during inspiration* the output of the right ventricle increased, while that of the left ventricle decreased. These changes were interpreted as due to (a) an inspiratory aspiration of blood into the right ventricle, and (b) a simultaneous increase in pulmonary vascular capacity such that the filling and output of the left ventricle decreased in inspiration.

These interpretations have now been tested under simplified conditions, using perfused terrapin hearts, heart-lung, and lung-heart preparations enclosed in an artificial thorax. During artificial inspiration (a) in the perfused hearts alone (simulating the mammalian right ventricle alone), filling and output increased, (b) in the heart-lung preparations (simulating right ventricle plus lungs), the increase in pulmonary vascular capacity exceeded the increased ventricular output so that blood flow *from* the lungs decreased, and (c) in the lung-heart preparations (simulating the lungs plus left ventricle), filling and output of the ventricle decreased.

In excised perfused dog's lungs placed in an artificial thorax, "inspiration" caused increases in pulmonary vascular capacity (varying from 20 to 29 cc. in 10-kgm. dogs) sufficient to accommodate the extra blood (varying from 18 to 32 cc. in 10-kilogram dogs) pumped by the right ventricle in inspiration.

The independence of the aural microphonic from auditory function. S. DWORKIN, J. E. HAWKINS, JR. (by invitation), M. H. LURIE (by invitation) and H. DAVIS. *Dept. Physiology, Harvard Medical School, Boston, Mass.* Three cats whose auditory thresholds had been determined by conditioned reflexes (CRs) were exposed under anesthesia to intense sounds. CR thresholds were again determined. The aural-microphonic threshold was determined and the ears fixed and examined histologically. In two animals in which damage was very slight and very extensive, respectively, there was excellent agreement among electrical audiogram, CR audiogram, and histological findings. The third showed a large (60 db) and nearly uniform loss of sensitivity by CR from 500 to 6000 cycles, with somewhat greater sensitivity for higher and lower frequencies. The aural-microphonic threshold was slightly and almost uniformly depressed (14 db) throughout the entire frequency range. Only a very small nerve component appeared in response to click stimulation. The organ of Corti appeared normal in the first turn but was completely absent in the second and third turns except for a small patch at the helicotrema. The small nerve component corresponds satisfactorily to the depressed CR function, but both were less than the state of the organ of Corti would suggest. The behavior of the aural microphonic does not correspond either to the histological picture or to the CR findings.

Other animals (dogs) with operative lesions have shown depressed aural microphonics in frequency bands that were heard normally by CR.

Cats exposed to equally intense sounds, but without anesthesia, showed no impairment of

auditory function or damage to the organ of Corti, probably due to the protective intra-aural reflex.

Further work on the utilization of the lower fatty acids. J. A. DYE and OLIVER L. BABCOCK (by invitation). *Dept. of Physiology, Cornell Univ., Ithaca.* The sodium salts of acetic, butyric, caproic, and caprylic acids (Eastman) were injected intravenously into nembutalized-nephrectomized dogs in amounts containing equivalent numbers of carbon atoms, namely, 12, 6, 4 and 3 mM per kgm., respectively. The injections were made in exactly 30 minutes, the rates of injection being such as to deliver equivalent numbers of carbon atoms per kgm. per minute. Curves of blood volatile fatty acids and blood ketone bodies were determined. The average times required for these fatty acids to disappear from the blood were 75, 165, 165 and 150 minutes, respectively. The corresponding average maximal blood ketone body levels were approximately equal for all except acetic acid, in which they occurred earlier and gave values only approximately one-half those of the others. According to the successive beta oxidation-acetic acid condensation hypothesis of fatty acid oxidation, these should yield equal quantities of ketone bodies. Since the utilization rate was faster for acetic acid, the ketone body production:ketone body utilization ratio and the blood ketone body levels might have been expected to be higher for acetic than for the other acids. Furthermore, if the fatty acids were first totally oxidized to acetic acid and this in turn conjugated into acetoacetic acid, the maximal rates of ketone body production would not be faster, but more likely slower, than those following the injection of equivalent quantities of acetic acid as such. The above theory does not explain the observed results.

The utilization of fatty acids by the extrahepatic tissues. J. A. DYE and ROGER W. MARSTERS (by invitation). *Dept. of Physiology, Cornell Univ., Ithaca.* The utilization of intravenously injected sodium salts of acetic, butyric, caproic, caprylic and capric acids by normal and abdominally-eviscerated dogs has been studied further. All animals were nembutalized and nephrectomized. In the eviscerated preparations, the extrahepatic tissues alone utilized an average of 60, 43, 39, 71 and 20 per cent as much of the respective fatty acids as did the normal animals. A marked rise of metabolism occurred in both groups and was measured quantitatively for acetic and butyric acids. For acetic acid the average excess oxygen consumption was equivalent to 49 per cent and 39 per cent of the theoretical amounts required to oxodize completely the acids which disappeared in normal and eviscerated animals, respectively. For butyric acid, these values were both 26 per cent. The specific dynamic action of injected fatty acids may not be 100 per cent of the theoretical amounts even though they were totally oxidized. These data offer indirect evidence that the utilization of these fatty acids was due, in part at least, to oxidation.

The development of functional nervous disturbances in thiamine deficient cats. GUY M. EVERETT (introduced by Dietrich C. Smith). *Dept. of Physiology, School of Medicine, Univ. of Maryland, Baltimore.* Observations were made on cats receiving a diet of autoclaved canned rabbit meat and yeast, supplemented by oral and intraperitoneal administration of riboflavin, pyridoxine, calcium pantothenate and alpha-tocopherol. Development of thiamine deficiency was essentially the same in the thirty animals studied.

After a week, anorexia is apparent and becomes progressively more severe with a concomitant loss in body weight. Except for slight weakness, behavior remains normal for the first three weeks. In the fourth or fifth week the cat suddenly develops head ventroflexion, circling movements, walking on a broad base, ataxia, marked extensor rigidity in the limbs and loss of body righting in air. During this stage any stimulus may precipitate a convulsive seizure lasting less than a minute. It begins with a violent sudden extension of the limbs and maximal head ventroflexion; clonus and writhing follow. The pupil is always dilated maximally and in some instances spontaneous nystagmus appears.

In less than an hour after intramuscular injection of thiamine, convulsions can no longer be elicited, walking improves and appetite returns. Within a day recovery is essentially complete.

The rapid onset of the syndrome observed and the dramatic recovery upon thiamine administration suggest a reversible biochemical change capable of producing profound and widespread functional nervous disturbances.

The constancy of body potassium on a high K diet. W. O. FENN, L. J. MULLINS (by invitation), TERRINE K. ADLER (by invitation), and LORRAINE HAEGE (by invitation). *Dept. of Physiology, School of Medicine and Dentistry, Univ. of Rochester, Rochester, N. Y.* An effort was made to determine to what extent the total potassium content of mice could be increased by feeding them on a very high potassium diet in which the potassium intake each day exceeded the total potassium content of the mouse.

Six mice with an average initial K content of 45.5 mgm. per mouse (4 control mice) were fed a high K diet for a period of 5-7 days. They consumed an average of 53 mgm. K daily and increased their final K content from 68.7 to 72.3 mM. K/kgm. The increase in final K content for three other mice with an initial content of 47.3 mgm. per mouse (3 control mice) and a daily in-

take of 54 mgm. K for 8 days was from 59.1 to 61.9 mM. K/kgm. Two mice with an initial (calculated) content of 46.2 mgm. increased their content from 59.1 to 65.6 mM./kgm. on a daily consumption of 77 mg. for 14 days. Two mice receiving daily intraperitoneal injections of 0.03 ml. cortin for 14 days consumed 81 mgm. K daily. Their initial (calculated) content was 49.6 mgm. and their final K content showed an increase from 59.1 to 66.9 mM. K per kgm.

Thus on the average 12 mice each weighing 19 grams ingested each day for 9 days 1.3 times as much K as they contained and thereby increased their weight 8 per cent and their K content per unit of weight only 7 per cent. A considerable part of this 7 per cent may have been in the g.i. tract so that the actual body K was scarcely changed.

Vagus thresholds and potassium tolerance in the turtle's heart. DOROTHY FETTER (by invitation), HELEN C. COOMBS and F. H. PIKE. *Dept. of Industrial Hygiene, Delamar Inst. of Public Health, Columbia Univ.* Observations, published previously, on the seasonal variations in the response of the turtle's heart in situ to excitation of the vagus, and on the response of the perfused excised heart to changes of concentration of potassium in the perfusion fluid, raise the question whether the response in the perfused heart bears any relation to the threshold of vagus excitation in that particular heart.

In two winter animals (February), in which the threshold of vagus excitation was first determined in situ, with subsequent perfusion of the excised heart, the low threshold of excitation of the vagus was correlated with low tolerance for excess of potassium in the perfusion fluid (Ringer), and a relative insensitivity to total lack of potassium. The heart stopped in from three to five minutes under excess of potassium, but continued to beat for twenty to thirty minutes when no potassium was present. It is in winter only that excess of potassium, combined with a cardiac glucoside, will stop the perfused heart in systole.

In three turtles, done in late June and July, with higher thresholds for vagus excitation, longer perfusion or greater concentration of potassium was required to stop the heart, while total withdrawal of potassium was soon followed by cessation of the heart beat.

Other experiments in spring, summer, autumn and winter have shown a similar sensitivity to excess of potassium with low threshold of vagus excitation, and greater tolerance to excess potassium when the vagus threshold was higher.

The effects of cardio-glycosides upon metabolism. ERNST FISCHER. *Dept. of Physiology, Medical College of Virginia, Richmond.* The effect of various digitalis glycosides, strophanthin, and ouabain upon tissue metabolism was studied by a statistical investigation of the in vitro oxygen consumption of tissue slices from normal rats, from rats therapeutically and slowly digitalized, and from rats slowly digitalized to a toxic saturation (severe anorexia). The results were fundamentally the same for all drugs employed. Since the largest number of experiments were performed with gitalin, figures are given only for that drug. Only toxic digitalization increases the vitro oxygen consumption of the heart (16.5 ± 3.2 per cent). Heart, brain, and liver from therapeutically digitalized rats have normal metabolic rates. Kidney metabolism is somewhat decreased (9.8 ± 4.5 per cent), while skeletal muscle metabolism is appreciably diminished (19.8 ± 1.4 per cent). Since the resting metabolism of the muscles represents a relatively large fraction of the total basal metabolism, it was to be expected that the latter would show a slight decrease after digitalization. Dogs were used for this type of experiments, but not all of them could be trained to keep quiet when breathing through a mask attached to a metabolism tester. However, those dogs which showed constant values from day to day before digitalization, had then a distinct diminution (12.7 ± 4.8 per cent) of basal metabolism which slowly returned to the original level after interruption of digitalization.

The effects of cardio-glycosides upon the arterio-venous O_2 and CO_2 differences and upon the CO_2 capacity of the blood. ERNST FISCHER and M. KATHARINE CARY (by invitation). *Dept. of Physiology, Medical College of Virginia, Richmond.* In dogs, the arterio-venous O_2 and CO_2 differences and the arterial CO_2 capacity were determined repeatedly before and after slow therapeutic digitalization (various digitalis glycosides, strophanthin, ouabain). The blood was drawn practically simultaneously from the femoral artery and vein, and from a subcutaneous vein. The arterial CO_2 capacity is slowly but constantly decreased by digitalization. Regularly in all dogs, but to a varying degree, the femoral O_2 and CO_2 arterio-venous differences are lowered by digitalization. However, the cutaneous O_2 and CO_2 differences are never lowered, but show often a tendency to increase. If such an increase in the cutaneous differences was distinct, the femoral differences were less diminished. These results might indicate that despite the decrease in femoral differences, the blood flow in the femoral artery is not increased but even diminished. Such a decrease in arterial blood flow would correspond to the diminished minute volume reported by others. This diminished minute volume is, however, not caused by any hypothetical damage to the healthy heart muscle by digitalis doses which are beneficial to a damaged heart, but by

the decreased circulatory need due to the diminished resting oxygen consumption of the muscles.

Yeast, thiamin and biotin on atrophy and regeneration of denervated skeletal muscle. ERNST FISCHER. *Dept. of Physiology, Medical College of Virginia, Richmond.* Yeast, thiamin or bioton given in excess to the Purina fox chow diet of rats older than 10 months has no effect upon the rate of atrophy of the denervated gastrocnemius, but the treated rats regained more quickly the weight loss caused by the operation. In younger rats, besides a much quicker operative recovery, the vitamins increase just perceptibly the weight gain for the next 3 to 5 weeks, but finally the controls reach the same weights as the treated rats. Two weeks after nerve section in young rats, atrophy is a little more pronounced in the treated rats than in the controls. This insignificant increase in atrophy can be explained by the quicker weight gain of the treated rats since denervated muscles participate less in growth than normal ones. Biotin, which increases considerably the growth of nerve fibers in tissue culture (H. L. Hamilton and H. Plotz. Proc. Soc. exper. Biol. and Med. 50: 133, 1942.), has even in young rats (15 units daily) little effect upon the outgrowth of central fibers after crushing of the sciatic nerve. Re-establishment of function judged as visible, fair, or good, occur in the average after 12.7, 15.1 and 22.3 days instead of after 13.8, 15.8 and 24.5 days. After 40 days, the maximal muscle forces (direct stimulation) were determined. The average recovery is slightly higher for the biotin rats, but so small as to be of no practical importance. Similar unimportant speeding of regeneration was observed in biotin treated dogs. Neither yeast nor thiamin increase the rate of nerve regeneration.

The influence of age and nutritional state upon the atropine treatment of the atrophy of denervated muscle. ERNST FISCHER and HARRY H. STOECKLE (by invitation). *Dept. of Physiology, Medical College of Virginia, Richmond.* In earlier experiments it has been demonstrated that atropine produces cachectic inanition of adult rats, in consequence of which the weight difference between denervated and so-called normal muscle is diminished, since the latter weighs considerably less than a true normal muscle (E. Fischer. Proc. Soc. exper. Biol. and Med. 51: 208, 1942). Repeating these experiments on rats of various ages, it was found that with decreasing age the inanition becomes less and changes finally into a strongly diminished growth rate. But also in the youngest rats, the apparent atrophy-retarding effect of atropine is due only to the fact that the so-called normal muscles weigh considerably less than the normal muscles of the controls. The atrophied muscles of the treated rats weigh on the average less than the atrophied muscles of the controls. The weight loss or the growth decrease of the treated rats can be diminished distinctly by feeding yeast or thiamin in large doses. The apparent atrophy retarding effect of atropine is more or less proportional to the final weight difference between treated and control rats. If by limitation of the food intake of the control rats, their weight curves were made similar to those of the treated ones, the atropine effect upon the atrophy practically vanishes. In the light of these experiments, the reported atropine retardation of atrophy in the monkey (S. Soskin and R. Levine. Am. J. Physiol. 138: 251, 1943) might not be a true retardation since the controls gained 10.5 per cent in weight during the observation period, and the treated animals only 2.5 per cent.

The rectal temperature of a group of mongrel dogs. M. H. F. FRIEDMAN and I. F. BENNETT (by invitation). *Dept. of Physiology, Jefferson Medical College, Philadelphia, Pa.* The rectal temperatures of a series of 107 mongrel adult dogs were taken by means of clinical rectal thermometers. These normal temperatures served as a basis for the evaluation of the pyrogenic effects of various tissue extracts. The thermometer bulb was inserted for a distance of 5 centimeters and readings taken after an interval of 3 to 5 minutes. During this time the dogs were quiet and did not pant or show signs of excitement. All animals were in apparent good health and free from distemper and mange. They were confined to their own quarters for at least one week before testing.

Twenty-two of the dogs were kept in air-conditioned quarters (environmental temperature about 74°F) and fed Purina dog chow daily and fresh meat several times per week. The rectal temperatures ranged from 100.2° to 103.8°, average 102.0°F. No significant differences between the sexes or between short and long-haired types were noted.

Eighty-five of the dogs were kept in a building which was not air-conditioned. These were fed Purina dog chow only. The rectal temperatures ranged from 99.9° to 104.8°, average 102.0°F. Not included in this series is one apparently healthy female with a rectal temperature of 96.4°F (verified by several readings during August). No significant differences between the sexes or hair lengths were noted.

Numerous temperature readings taken on each of six female dogs throughout the academic year showed various degrees of individual variations. The widest range was 99.9° to 102.8°F, the narrowest 100.2° to 100.7°F.

Phosphate exchange in resting cardiac muscle in vitro as indicated by radioactivity studies: III. ROBERT F. FURCHGOTT (by invitation) and EPHRAIM SHORR (with the technical assistance of Gladys Brewer). *New York Hospital and the Dept. of Medicine, Cornell Univ. Medical College,*

New York City. A previous report from this laboratory showed the following relative specific radioactivities for phosphate fractions of dog cardiac slices after 30 minutes incubation at 37.5° in oxygenated M/75 phosphate-Ringer containing $P^{32}O_4$: phosphate of medium, 100; extracellular inorganic phosphate (IP_1), 100; intracellular inorganic phosphate (IP_2), 20; creatin phosphate (CP), equal to IP_2; pyrophosphate, 70 per cent of IP_2; difficultly hydrolyzable phosphate, 20 per cent of IP_2.

The pyrophosphate fraction has been found to consist of adenosine triphosphate (ATP) and diphosphate. The specific radioactivity of the terminal phosphate of ATP in the pyrophosphate fraction was then determined separately by a lobster muscle preparation capable of enzymatically liberating only this group from ATP, and found equal to that of IP_2 and CP after 30 minutes incubation with $P^{32}O_4$.

These equalities in specific radioactivity might be explained as follows: 1, a slow exchange between IP_1 and IP_2; 2, a rapid phosphorylation cycle (energized by coupled oxidations) from IP_2 through the terminal phosphate of ATP; 3, a rapid equilibrium exchange between terminal phosphate of ATP and CP. This would provide a rapid metabolic mixing cycle, bringing the specific radioactivities of IP_2, CP and terminal phosphate of ATP to the same values.

Evidence against the formation of an organic phosphate intermediate in the passage of phosphate from IP_1 to IP_2 is provided by results of 30 minute incubations with $P^{32}O_4$ at 2°C. or under anaerobiosis, conditions which reduce phosphorylations. Under these conditions the specific radioactivity of IP_2 is much higher than that of any of the above organic phosphate fraction. [*This study was aided by a Grant from the Carnegie Corporation. The radioactive phosphorus was kindly supplied by Dr. J. H. Lawrence of the Radiation Laboratory, University of California, Berkeley.*]

Inhibitory effects in auditory-nerve fibers. R. GALAMBOS. *Dept. of Physiology, Harvard Medical School, Boston, Mass.* As reported earlier, many single auditory-nerve fibers discharge continuously at a slow rate ("spontaneous" activity). Furthermore, every fiber is characterized by having a "response area" defined by those frequencies and intensities which increase the rate of discharge over the spontaneous, or initiate activity in those not displaying spontaneous activity.

In some fibers discharging spontaneously, tones outside the response area reduce or abolish the activity. The same phenomenon is observed in some fibers responding to adequate tones upon presentation of a second tone lying outside the response area. In both cases tones just above the high frequency limit of the response area are usually particularly effective, but this is not invariably the case.

Not all fibers of the auditory nerve behave in the manner just described. Those which do, however, give clear evidence of a decrease of auditory-nerve activity upon presentation of acoustic stimulation.

Presumably the nerve impulses in question originate peripheral to the electrode, but the possibility that they represent centrifugal impulses in the auditory nerve is not yet ruled out. In any event these findings indicate the presence of at least 2 types of auditory-nerve fibers, differentiated on the basis of whether or not their response to one tone is modified by the presence of a second tone. They also suggest that pitch discrimination may involve a factor of nervous interaction within or closely associated with the inner ear itself.

Functional organization and inter-hemispherical relations: medial aspect of frontal lobe in chimpanzee. HUGH W. GAROL and EDWARD W. DAVIS (introduced by W. S. McCulloch). *Illinois Neuropsychiatric Inst.* By local strychninization and recording electrical activity the functional organization and inter-hemispherical connections of the medial aspect of the frontal lobes have been determined in the chimpanzee.

The cortex anterior to area 4 contains ten areas. Rostrad on the gyrus marginalis lie areas 4s, 6, 8s, 9, 32, 10, 12 and 11; on the gyrus cinguli, areas 24s and 32.

The largest, 32, extends along the sulcus cinguli superior to 24s and antero-dorsally to the sagittal margin, bounded posteriorly by 9 and anteriorly by 10.

Homolaterally, area 4s fires 32 and suppresses cortical electrical activity generally. Area 6 fires itself widely and all posterior portions of the sensory cortex. Area 8s fires 32 and suppresses cortical electrical activity generally. Area 9 fires only itself. Area 32 fires itself throughout and, posteriorly, 31. Area 10 fires itself locally. Area 12 fires itself and 32. Area 11 fires only itself. Area 24s fires 32 and suppresses cortical electrical activity generally. N.B. Area 32 is fired also from suppressor areas 2s and 19s—i.e., area 32 is fired by all suppressor areas.

With the exception of areas 8s, 4s and possibly 24s, all these areas fire contralateral homoiotopic points.

Of the areas considered, only 8s, 4s and the new suppressor area, 24s, fire the nucleus caudatus.

The vasopressor and mydriatic action of some phenylethyl amines. C. W. GEITER (by invitation) and A. M. LANDS. *Frederick Stearns and Company, and Wayne Medical College, Detroit.* In this investigation the hydrochlorides of the following were used: ethyl-beta-phenylethyl amine (I), allyl-beta-phenylethyl amine (II), diethyl-

beta-phenylethyl amine (III), dibutyl-beta-phenylethyl amine (IV), methyldi-beta-phenylethyl amine (V), ethyldi-beta-phenylethyl amine (VI), propyldi-beta-phenylethyl amine (VII) and tri-beta-phenylethyl amine (VIII). Compound I, 0.05 mgm./kgm., injected intravenously into dogs anesthetized with nembutal, produced a rise in carotid pressure. Doses of 0.5 mgm./kgm. induced rises of 30–80 mm. Hg lasting 10–20 minutes. Doses of 0.5–2 mgm./kgm. produce an initial but transient fall followed by the sustained rise in pressure. These responses are not potentiated by cocaine. Compounds II, VII and VIII were without effect on blood pressure, III and VI caused a transient fall and V usually caused a fall although in a few instances the fall was followed by a slight rise. Compound IV caused a transient fall, followed again by a slow reduction in blood pressure. Doses as large as 0.5 mgm./kgm. sometimes caused death.

In the unanesthetized dog, the subcutaneous injection of 0.5–1 mgm./kgm. of compound I gave a rise in systolic blood pressure of 15–25 mm. Hg within 20–40 minutes and lasting 60–80 minutes. A bradycardia of 15 to 30 beats/minute was observed at the peak of the pressure. The heart rate returned to normal somewhat more slowly than did the blood pressure. A 2 per cent solution of compound I instilled into the human conjunctival sac caused a maximum degree of mydriasis within 2 hours with some pupillary dilatation for over 4 hours. Intravenous injection of 20–30 mgm./kgm. into unanesthetized albino rabbits caused moderate mydriasis, lasting about 30 minutes.

Compound I has a low toxicity. Subcutaneous doses of 300–800 mgm./kgm. caused only an occasional death. Intravenous injections of 75 mgm./kgm. as a 2 per cent solution into albino rabbits were tolerated.

Further studies on the influence of insulin coma on conditioned reactions in rats. E. GELLHORN and H. MINATOYA (by invitation). *Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.* Conditioned reactions (jumping from compartment A to compartment B in response to a bell preceding by two seconds the unconditioned stimulus) which had been inhibited by lack of reenforcement can be restored by insulin hypoglycemia. Insulin hypoglycemia is most effective when it causes coma (absence of righting reflexes) whereas lesser effects result from insulin convulsions or precomatose states. Properly timed comas may cause permanent recovery of previously inhibited conditioned reactions. The effects are specific inasmuch as other than the conditioned stimuli fail to cause any reactions. Rats only partially conditioned and then subjected to insulin coma show a much higher degree of conditioning than similarly treated control animals injected with sodium chloride. The experiments show that insulin coma exerts chronic effects which consist not only of the removal of intracentral inhibitions in the Pavlovian sense but also facilitate those excitatory processes which are the basis of conditioning. [*Aided by the John and R. Markle Foundation.*]

The effect of insulin coma on differentiated conditioned reactions of the rat. E. GELLHORN and K. SEESE (by invitation). *Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.* The observations of Rosen and Gantt (Trans. Am. Neurol. Soc. 1942, p. 41) that repeated metrazol convulsions resulted in a dedifferentiation and final loss of conditioned reflexes in dogs prompted a similar investigation concerning the effect of insulin comas on negative (inhibitory) and positive (excitatory) conditioned reactions (c.r.) in rats. Two to three conditioned reactions were established in which a bell, a sound of 250 vibrations/second and a light were used as conditioned stimuli (c.s.). One or two conditioned stimuli were made inhibitory by lack of reenforcement whereas a third c.s. was reenforced until it caused a c.r. in about 100 per cent. In such animals insulin coma regularly restored the inhibited reactions without altering the response to the positive c.s. The effect on the inhibited reactions was reversible after several days. In no instance was a decrease on the response to positive c.s. found after insulin coma. When the response to one conditioned stimulus was 35 to 50 per cent and to another 0 per cent, insulin coma raised the c.r. in both cases but more so in the former. It is concluded that insulin coma does not diminish the response to positive c.s. under conditions which lead to a reversible restoration of inhibited c.r.

Eserine, acetylcholine and atropine in nervous integration. ROBERT GESELL and ELWOOD T. HANSEN (by invitation). *Dept. of Physiology, Univ. of Michigan.* Among the outstanding observations on eserine were 1, a reinforcement of thoracic expiratory contractions; 2, a temporary irregularity of strength of torsal inspiratory contractions associated with subnormal pulmonary ventilation; 3, an initiation and strengthening of the facial accessory respiratory muscles.

These effects occur with vertebral injections after chemoceptor denervation and are therefore central.

Irregularity of breathing consisted of shallow breaths tending to weaken and of sporadically deep breaths tending to strengthen as eserine poisoning increased.

Large injections intensified all effects of eserine including the curtailment of the more shallow breaths. Complete curtailment left the powerful inspirations separated by apneas of variable durations.

Corresponding apneas were absent in the facial rhythm. Respiratory block is indicated.

Increasing intensity of costal expiratory, of torsal inspiratory and of facial accessory inspiratory contractions are thought to indicate a progressive pooling of acetylcholine at all nerve stations where bombardment and release of acetylcholine occurs.

Failure of the smaller inspirations to attain maximum intensity is attributed to a disproportionate potentiation of expiratory neurones structurally coupled with their opposing inspiratory neurones. Only those inspirations breaking free of the dominating reciprocal inhibition are thought to gauge the potential activity of the inspiratory cells.

The effects of eserine were duplicated with slowly injected extrinsic acetylcholine.

Atropine produced profound central effects: 1. reversal of the response to eserine and extrinsic acetylcholine and 2, diminution of breathing motivated by intrinsic acetylcholine (eupnea and reflexogenic hyperpnea). Antagonism was greater to extrinsic than to intrinsic acetylcholine.

It is thought that the support which our experiments give to the humoro-electrical theory of nerve cell function may prove basic to neurophysiological concepts.

A possibility of an axone reflex originating at the motor end plate of striated muscle. ROBERT GESELL and JOHN FINERTY (by invitation). *Dept. of Physiology, Univ. of Michigan.* The sartorius muscle of the frog immersed in a weak solution of acetylcholine responds with a serrated contraction in which small and frequent shortenings of a relatively uniform rhythm are superimposed upon a greater sustained shortening. It is hardly conceivable that a single muscle fiber would have sufficient strength to produce the rhythmic contractions. Fifty or more fibers beating synchronously through the intermediation of an axone reflex offered by a single neuraxone might however have sufficient power. Such a reflex could be initiated at any motor end plate infiltrated with sufficient acetylcholine to establish electrotonic currents of threshold value. Three circuits are possible, two through the muscle, one on each side of the motor end plate, and one through the nerve fiber ending in the motor end plate. If an impulse is initiated in the nerve fiber it would spread via axone reflex to all muscle fibers on the circuit. This concept is supported by the recording of antidromic impulses in an acetylcholine stimulated muscle (Masland and Wigton, J. Neurophysiology **3:** 269, 1940). Action potentials of contracting muscle could be another source of initiation of an axone reflex.

Analgesic effect of dextro-amphetamine alone and in combination with morphine sulphate. F. R. GOETZL (by invitation), D. J. BURRILL (by invitation) and A. C. IVY. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* Pain responses were obtained by applying uninterrupted alternating current of variable voltage to the cuspid teeth of 10 dogs through silver amalgam fillings. Upon administration of analgesic drugs the voltage required to produce a response was increased over a period of 90 minutes. Dextro-amphetamine (1 mgm. per kilo) was a more effective analgesic than morphine sulphate in the same dose. Dextro-amphetamine (1 mgm. per kilo) and morphine (0.5 mgm. per kilo) in combination were still more effective, and the amphetamine largely prevented the drowsiness due to the morphine. The drugs and combinations used, the dosage, and the analgesic effect in terms of percentage of the original voltage required for response are, in order of increasing analgesic effect, as follows:

Drug and dose	*Mean % all voltages* (Initial voltage = 100%)
None—control	99.76
0.5 mgm. morphine sulphate, per kilo	109.82
1.0 mgm. morphine sulphate, per kilo	121.58
1.0 mgm. d-amphetamine, per kilo	135.63
0.5 mgm. morphine plus 0.5 mgm. d-amphetamine, per kilo	140.00
0.5 mgm. morphine plus 1.0 mgm. d-amphetamine, per kilo	156.68

Effect of low pressures on thyrotropic and gonadotropic hormone production in the rat. ALBERT S. GORDON, FRANK J. TORNETTA (by invitation), SAVINO A. D'ANGELO (by invitation) and HARRY A. CHARIPPER. *Dept. of Biology, Washington Square College of Arts and Science, New York Univ., New York City.* Adult male rats were exposed to low pressures of 250–280 mm. Hg (25–28,000 ft.) 6 hrs./day for 14–18 days. Pituitaries and blood sera collected from such animals were pooled and tested for thyrotropic content in the young, starved tadpole (method of D'Angelo, Gordon and Charipper. Endocrinology **31:** 217, 1942). Intraperitoneal injections of 0.05 cc. of the sera and pituitary suspensions were made into tadpoles on alternate days and the rate of metamorphic advance noted. Low pressures were found either to increase the thyrotropic content of the pituitary or not to affect it at all. In no case was a decrease in potency noted. On the other hand, blood sera from low pressure-subjected rats contained significantly smaller quantities of thyrotropic hormone than sera from normal rats.

The gonadotropic content of pituitaries from rats exposed to the same low pressures (6 hrs./day for 14 days) was determined by injecting finely cut glands suspended in dilute NaOH into immature rats (method of Reece and Weatherly. Proc. Soc. Exper. Biol. and Med. **49:** 218, 1942). Such glands possessed a 40–60 per cent greater potency than those from normal rats. This assay method failed to detect gonadotropic hormone in the blood sera

of either normal or low pressure-exposed rats despite the injections of large doses. Pituitary glands from rats subjected to low pressures 18–20 hrs./day for 10–12 days possessed a considerably lower gonadotropic potency than normal glands. Since these animals lost considerable weight, it is difficult to tell whether this result is due to the longer period of anoxia or to the chronic inanition.

The determination of thiourea in serum. ARNOLDUS GOUDSMIT. *Division of Biochemistry, The Laboratories, Philadelphia General Hospital, Philadelphia, Pa.* The study of the total water content of the intact animal body has been hampered by the absence of a suitable method for its determination. The use of thiourea, because of its structural similarity to urea, has been suggested. However, no practical procedure for its estimation in sufficiently small amounts has been available to study its distribution in the water of the body.

The method developed allows the determination of thiourea in 2 cc. of human serum. A 1:4 protein-free filtrate is prepared by the addition of sodium tungstate and sulfuric acid. To the centrifugalized filtrate is added an equal volume of a dilute, buffered, Grote's reagent. The latter is prepared by mixing one part of Grote's reagent (J. Biol. Chem. 93: 25, 1931) with four volumes of a sodium hydroxide-potassium chloride buffer, so as to obtain a pH of approximately 10.75 in the final solution.

A red color develops in the course of one to two hours. The relationship of light absorption to concentration of thiourea follows Beer's law closely. Colorimetric readings, using a filter with a maximum transmission at 560 millimicrons, were made on a variable layer photoelectric photometer. In a set of ten consecutive duplicate analyses in which the concentration ranged between 1.6 and 2.4 mgm. of thiourea per 100 cc. of serum recoveries varied between 98.9 and 100.9 per cent, with an average of 99.8 ± 0.7 per cent.

The effect of diet on the action of certain sulfonamides.[1] ESTHER M. GREISHEIMER, ROBERTA HAFKESBRING and GRACE E. WERTENBERGER (by invitation). *Woman's Medical College of Pennsylvania.* Male rats, at weaning age, were placed on special diets. Three weeks later, one dose of sulfonamide was given by intraperitoneal injection, and the animal killed after three hours. Blood sugar, liver glycogen and drug blood level were determined.

Purina chow checkers was chosen as the control diet. The other diets studied to date are high fat and high protein, in which butter and casein form about 88 per cent of the total caloric value, respectively. Adequate salt mixture and vitamin supplements are added. The average daily gain in weight is approximately 3 grams on the control diet, 2 on high fat and 1½ on high protein.

The sulfonamides studied to date include the sodium salts of sulfapyridine, sulfadiazine and sulfathiazole.

Sodium sulfapyridine causes a marked increase in blood sugar on all diets, the greatest effect being noted on the high fat diet. This drug also causes a pronounced decrease in liver glycogen, least marked on the high fat diet. Although the total drug is slightly higher on the fat diet, the amount of conjugation is less, and this may serve to protect the liver glycogen in some measure.

Sodium sulfadiazine has little effect on blood sugar, but causes a moderate reduction in liver glycogen; little conjugation takes place.

Sodium sulfathiazole has less effect on liver glycogen than the other two drugs, although more conjugation takes place.

Gelatin as a blood substitute in shock due to limb trauma. F. S. GRODINS (introduced by A. C. Ivy). *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* Shock was produced in etherized dogs by trauma to an extremity. A sustained drop in blood pressure to 70 mm. Hg or less was taken as an indication of shock. After the blood pressure had remained at the shock level for about 30 minutes, 0.9 per cent sodium chloride solution, normal dog plasma, or 5 per cent gelatin-saline (pH 7) was given intravenously in an amount equal to 50 per cent of the calculated blood volume of the animal. The blood pressure was then followed for some hours.

In 10 animals treated with 0.9 per cent saline, the blood pressure rose fom an average shock level of 44 mm. Hg to 94 mm., but the effect was sustained only for 45 minutes. In 10 animals treated with plasma, the pressure rose from 54 mm. Hg to 135 mm. and the rise was maintained for about 2¼ hours. In 10 animals treated with 5 per cent gelatin-saline, the blood pressure rose from 54 mm. Hg to 135 mm. and the rise was maintained for about 2¼ hours. These results show that a 5 per cent gelatin-saline solution is much more effective than 0.9 per cent sodium chloride and is about equal to normal blood plasma in its ability to produce a sustained rise in blood pressure in animals suffering from shock due to limb trauma.

The gelatin solution used in this study was found to produce darkening of the blood, agglutination of the red blood cells, and a rapid sedimentation rate *in vitro* and *in vivo*. The significance of these findings in relation to the use of gelatin as a blood substitute is discussed in a separate communication.

The preparation of a subcutaneously effective enterogastrone concentrate. HARRY GREENGARD, M. I. GROSSMAN (by invitation), A. P. HANDS (by invitation) and A. C. IVY. *Dept. of*

[1] Aided by grant 475, Council on Pharmacy and Chemistry, American Medical Association. The sulfonamides used in this study were supplied by Lederle Laboratories, Inc.

Physiology, Northwestern Univ. Medical School, Chicago. Previously reported enterogastrone concentrates have been found uniformly potent only when administered by the intravenous route, except in very large doses. Purification of this material has been effected by precipitation with picric acid and treatment of the resulting insoluble picrate with acidified 70 per cent acetone. This procedure leaves as an insoluble inactive residue about 50 per cent of the material. The filtrate is precipitated with acetone, collected by centrifugation, washed, dissolved with water, and treated with an excess of aniline. The material left in solution after the aniline treatment is precipitated with acetone, the precipitate centrifuged out, washed, and dried. The product obtained from this procedure is a colorless powder, easily soluble in water, and injectable subcutaneously in 10 per cent solution without causing any evidence of pain. It is uniformly potent in depressing gastric secretion in a dosage of 20 mgm. by the intravenous route, or in a dosage of 50 mgm. subcutaneously. [*Aided by a grant from the Josiah Macy Jr. Foundation.*]

Dietary composition and pancreatic enzymes; the effect of predigested dietary constituents. M. I. Grossman (by invitation), Harry Greengard and A. C. Ivy. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* We have hown that a marked increase in the protein or the tarch content of an adequate diet administered to rats over a 21-day period will markedly affect the composition of the animal's pancreatic enzymes. The effect is to increase the production of the enzyme acting on the predominant component of the diet, the mechanism of which may be a "demand" factor occasioned by the presence of undigested food in the intestine, or a humoral agency operating through a temporary high concentration of digested products in the circulation during the absorption period. In the former case, substitution of a predigested constituent in the diet should inhibit production of the appropriate pancreatic enzyme; in the latter, it should enhance it, since digestive products are being absorbed rapidly in a short period of time. When these hypotheses were tested by substitution of an equal amount of a complete amino acid mixture for casein, and of an equal amount of glucose for starch, it was found that there was an increased trypsin content of the pancreas in the former instance, and an increased amylase content in the latter. It is concluded that the mechanism of adaptation of the pancreatic enzymes to dietary constituents is a humoral one, and takes place as a result of the relative concentrations of products of digestion during the absorptive phase.

The effect of vitamin B complex deficiency on the water content of the body and various organs of the albino rat. John Haldi, Glenville Giddings (by invitation) and Winfrey Wynn (by invitation). *Dept. of Physiology, Emory Univ., Ga.* The skin and body of albino rats fed a vitamin B complex free ration for 28 days contained more water per unit of tissue than the skin and body of their litter mate controls on the same ration to which a liberal amount of yeast was added. The animals were allowed to eat ad libitum. The experimental animals lost approximately 23 per cent of their original weight whereas the controls gained about 35 per cent. The percentage water of the body was 5.5 per cent higher on the B free ration in the males and 5.9 per cent higher in the females. The larger percentage on the B free ration, however, was shown to be due to the lowered food intake resulting from the vitamin deficiency and not directly to the lack of the B complex. In a second series of experiments in which the caloric intake of the experimental and control animals was equalized the percentage water content was the same on the two rations. The amount of water in the brain, liver, kidney and muscle was the same in the experimental and control animals both when they were allowed to eat ad libitum and when the caloric intake was equalized.

Prevention of experimental gastrojejunal ulcer by enterogastrone. A. P. Hands (by invitation), Harry Greengard, G. B. Fauley (by invitation) and A. C. Ivy. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* It has been previously reported by us (Endocrinology 30: 905, 1942) that an enterogastrone concentrate effective in inhibiting gastric secretion will prevent the development of gastrojejunal ulcer in the Mann-Williamson dog in 80 per cent of cases when injected intravenously. Withdrawal of the therapy at the end of a year did not result in the development of an ulcer. Eight animals are at present alive and in excellent condition for a period of from 9 to 17 months without therapy, or a total of 21 to 29 months after operation. The means whereby enterogastrone renders these animals resistant to ulcer formation is at present unexplained.

A second series of animals has been studied, using as a therapeutic agent a more highly purified enterogastrone concentrate effective by the intramuscular or subcutaneous route. The nine dogs thus treated have been maintained in good condition for a period of 20 weeks after operation, or 4 weeks longer than the average time in which an ulcer develops in the untreated Mann-Williamson dog. The enterogastrone concentrates have no anaphylaxis-producing property. [*Aided by a grant from the Josiah Macy Jr. Foundation.*]

A possible anticholinesterase action of ammonium chloride. Elwood T. Hansen (by invitation), Robert Gesell and Charles R. Brass-

FIELD. *Dept. of Physiology, Univ. of Michigan.* Ammonium chloride produces a respiratory response strikingly similar to that of eserine (see Gesell and Hansen in these Proceedings) but differing in detail from the response to carbon dioxide. If the similarity of effects of ammonium chloride and eserine are based on an increase of anticholinesterase activity it becomes essential to discover why two different types of acidosis produce characteristic effects on breathing. It is conceivable that the characteristic effects may be linked with slightly differing relationships of internal to external pH, to the NH_4 radical or to some other factor.

The renal excretion of chloride and water by the normal dog. KENDRICK HARE and RUTH S. HARE (by invitation). *Dept. of Anatomy, State Univ. of Iowa, Iowa City.* Chloride excretion has been followed in normal dogs before, during, and after intravenous infusion of saline solutions ranging in concentration from 0.3 per cent to 5.0 per cent. Simultaneous creatinine clearances permitted calculation of chloride filtration and reabsorption. Chloride and water reabsorption have been correlated and for convenience expressed as milligram per cent although it is probable that this value does not represent the actual concentration of chloride in the reabsorbed water (Walker et al. Am. J. Physiol. 134: 580, 1941), but is the resultant of several reabsorptive processes. The ratio of concentration of chloride in the tubular reabsorbate to that in plasma has been designated the chloride R/P. This ratio, normally one, increases when hypotonic saline is given intravenously or when water is given by mouth; the administration of iso- or moderately hypertonic saline (1.5 per cent) has no effect; but the injection of 2.0 to 5.0 per cent NaCl causes the ratio to decrease from unity to 0.95–0.91 (Rehberg Biochem. J. 20: 561, 1926). When saline infusions of different concentrations were given at the same rate to the same dog in successive experiments, a family of curves was obtained by plotting the chloride R/P against time. The configuration of each curve is quite characteristic of the concentration of the saline infused.

The pituitary control of the renal excretion of chloride and water. RUTH S. HARE (by invitation), KENDRICK HARE and DONALD PHILLIPS (by invitation). *Dept. of Anatomy, State Univ. of Iowa, Iowa City.* The chloride R/P of dogs with diabetes insipidus is greater than one, and the infusion of a graded series of NaCl solutions (0.3–5.0 per cent) does not cause any consistent variation. This difference in the response of the polyuric and of the normal dog suggests that the neurohypophysis regulates the partition of water and chloride between tubular reabsorbate and urine. This suggestion has been supported by the following experiments: 1, the addition of Pitressin to the infusion fluid (2.5 per cent NaCl) so that the rate of administration of the hormone was 60–720 milliunits per hour partially restored the response to normal. The rate of chloride excretion was not elevated by even the largest dose of Pitressin, but a reduction in water excretion, closely related to the dose of Pitressin was regularly obtained. Pitressin, therefore, lowers the chloride R/P by facilitating the tubular reabsorption of water, but has no demonstrable effect on the reabsorption of chloride. 2. The elevated chloride R/P that results from the infusion of hypotonic salt solution into normal dogs is returned to normal by the simultaneous infusion of 1.7–5.0 milliunits of Pitressin per hour. This, in light of an elevated chloride R/P in dogs with diabetes insipidus, is evidence of inhibition of the neurohypophysis by hypotonic salt infusions. The depressed chloride R/P of the normal dog when 2.0–5.0 per cent salt is infused is evidence of increased liberation of the antidiuretic hormone since destruction of the neurohypophysis eliminates the response and replacement therapy with Pitressin restores it.

The relation between desoxycorticosterone acetate and diabetes insipidus in the rat. ALDEN S. HARNED (by invitation) and WARREN O. NELSON. *Wayne Univ. College of Medicine, Detroit.* Attention has been called to the production of a condition simulating diabetes insipidus by long term administration of DCA. An investigation was undertaken in which the water balance was studied in groups of rats under the following conditions: normal (N), adrenalectomized (AD), diabetes insipidus (DI) (lesions placed in region of median eminence with Horsley-Clarke stereotaxic instrument), adrenalectomized-d.i. (ADI), hypophysectomized-d.i. (HDI), and hypophysectomized with lesions but no d.i. (H).

Urine output without treatment was recorded (H_2O). The animals were then given either 0.5 per cent NaCl instead of drinking water (NaCl) or 3 mg. DCA per day (DCA) and following this period were given the two in combination (Both). The results for urine output are recorded in the accompanying table in cc. as averages for periods of at least five days.

	N	AD	DI	ADI	HDI	H
H_2O	10	10	43	43	30	29
NaCl	19	19	147	93	32	33
DCA..... ...	17	—	(231)	73	—	—
Both	88	69	320	320	48	37

DCA produces an increase in water exchange in all except hypophysectomized animals and is particularly effective in combination with NaCl. While this was most marked in normal animals, the basic output of d.i. animals is so large that physiologic limitations might impede a com-

parable increase. However, the percentage increases within these groups are so close as to indicate that there is little relationship between the DCA-NaCl increase and the primary presence or absence of diabetes insipidus.

The figures for DCA in uncomplicated d.i. (in parentheses) may not be significant since they represent a single animal. The absence of effect in hypophysectomized animals is interesting, but as yet without satisfactory explanation.

Electrocardiographic observations in mental patients receiving large doses of acetylcholine intravenously. MEYER M. HARRIS and BERNARD L. PACELLA (introduced by S. E. Barrera). *Dept. of Internal Medicine and Psychiatry, New York State Psychiatric Inst. and Hospital.* Electrocardiographic observations were made in eight mental patients receiving a freshly prepared 10 per cent solution of acetylcholine intravenously in doses ranging from 60 to 500 mgm. injected rapidly within a few seconds. Records were obtained immediately before, during, and immediately following the injection of acetylcholine. A Cambridge Research Type of String Galvanometer was used for recording the effect of the injections. The dose of acetylcholine was increased gradually until cardiac arrest lasting 30 to 45 seconds with loss of consciousness and convulsions was produced. (A means of convulsant shock therapy.) The dose required to produce this effect varied from 220 to 500 mgm. and bore no relation to the weight of the patient.

The electrocardiograms showed the following changes. In some cases even small doses of acetylcholine (60 mg.) produced a short period of bradycardia during which time the P waves disappeared from the complexes. This was then followed by a period during which the P waves were inverted. In other cases only the very large doses of acetylcholine which brought about cardiac arrest for approximately 30 seconds resulted in a disappearance of the P waves in only a few of the complexes following the resumption of the heart beat. The susceptibility of the auricles to acetylcholine showed marked variability in different patients. These findings were in contrast to the asystole of the auricles observed by some investigators using very small doses of acetylcholine in animals.

Spontaneous resumption of the heart beat occurred in all the cases studied.

A paradoxical effect of urogastrone and enterogastrone. S. C. HARRIS (by invitation), J. H. HUSTON (by invitation), and A. C. IVY. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* It is generally accepted that the preparations known as urogastrone and enterogastrone are inhibitors of gastric activity.

Both preparations inhibit the gastric secretory response to histamine in the intact and total pouch stomach when given intravenously or subcutaneously. Both preparations also inhibit the gastric motility initiated and maintained by the distention of the recording balloon.

We have found, however, that preparations of urogastrone and enterogastrone which do inhibit gastric motility in the intact stomach are devoid of activity in motor studies on the vagotomized stomach. These findings were controlled by effectively inhibiting motility in the vagotomized stomach by introducing fat into the intestine and by injecting pituitrin in minute quantities. [*Aided in part by a grant from the Committee on Endocrinology of the National Research Council.*]

The hypertensinogen concentration of the plasma of patients with various diseases. FLORENCE W. HAYNES and LEWIS DEXTER (by invitation). *Medical Clinic of the Peter Bent Brigham Hospital, and the Dept. of Medicine, Harvard Medical School, Boston.* Previous determinations of the concentration of plasma hypertensinogen, the globulin substrate of renin, in hypertension have been supplemented by its determination in 33 patients with various diseases and in 8 normal subjects. Two to 4 cc. of non-hemolyzed human plasma were incubated for 25 minutes at 37 degrees C. at pH 7.3 with an excess of human renin (approximately 50 cat units). Assay was performed on anesthetized cats by comparing the blood pressure rise obtained with that of a standard hypertensin solution, as described by Braun-Menendez and co-workers. The normal concentration of hypertensinogen usually lies between 2 and 5 cat units (0.5 and 1.25 dog units) per cc.

In 3 of 4 patients with signs of hepatic insufficiency, the hypertensinogen concentration was about one half normal. Of 12 patients with renal insufficiency and azotemia, 8 with high serum globulin values, and 10 with fever, the hypertensinogen concentration was normal except in 5 cases. In 2 with azotemia and in one moribund patient with high fever, values were nearly twice normal, whereas in 2 of those mentioned with liver disease they were low. Hypertensinogen concentration was normal in the following cases: One each of Addison's disease, Hodgkin's disease, ulcerative colitis, leukemia and obesity, 2 cases of cardiac failure, and 5 with normal blood pressure under ether anesthesia. The concentration of hypertensinogen in plasma is therefore essentially normal in patients with hypertensive vascular disease (previously reported), renal insufficiency, anesthesia, and miscellaneous disorders, but often significantly decreased in hepatic insufficiency. [*Aided in part by grants from the Markle Foundation and the Armour Laboratories.*]

The permeability of the toadfish liver to inulin, with and without choleretics. CHARLOTTE HAYWOOD. *Dept. of Physiology, Mount Holyoke Col-*

lege, South Hadley, Mass. For evaluating liver permeability, passage of the lipoid-insoluble inulin molecule (M.W. 5100) into the bile has been studied in the living toadfish (Opsanus tau), whose aglomerular kidney cannot eliminate it.

A day or more after intramuscular injection of about 2 grams inulin per kgm. body weight, hepatic bile was collected from a cannula inserted into the emptied gall-bladder. During operative and collection periods immobilization and adequate respiration were maintained. Bile and protein-free serum were analyzed for inulin as levulose, by Shaffer and Somogyi's micromethod, modified, following hydrolysis. Control experiments on normal bile and serum gave correction factors for experimental samples.

In 24 experiments without choleretics, bile flows averaged 22.8 mgm. per hour. Inulin was always found in the bile after injection, though less concentrated than in serum; bile/serum inulin ratios ranged from 0.23 to 0.85, averaging 0.57. Eighteen experiments with choleretics (sodium dehydrocholate and sodium taurocholate) gave, in comparison, bile/serum inulin ratios which ranged from 0.03 to 0.35, averaging 0.18. In experiments where a period with choleresis followed one without it, the bile inulin dropped usually to 30 or 40 per cent of the earlier value. Increased rates of bile flow, however, tended to increase the hourly elimination of inulin.

The experiments without choleresis indicate considerable permeability, probably intercellular. Further study is needed to determine whether the choleretics act through an altered size relationship between molecule and intercellular pore, or simply through an increased passage of water.

Somatic motor responses produced by electrical stimulation of the cerebral cortex of new-born and young kittens. EARL W. HENRY (introduced by Clinton N. Woolsey). *Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* Sixty-cycle sine-wave stimulation was employed to determine the responses elicitable from the "motor" cortices of new-born and young kittens. The purpose in mind was to examine in this way maturation of the "motor" cortex and to correlate results with observations on development of placing and hopping reactions in kittens. Weed and Langworthy (1926) had reported that electrical stimulation of the kitten brain produced forelimb movements at birth, hindlimb movements at 16 days and facial-masticatory movements at 21 days.

In the present experiments 28 kittens, ranging in age from new-born to 11 days, were examined. It was found that localized responses of all parts of the body musculature (facial-masticatory, foreleg and hindleg) could be obtained at birth as well as at later ages by stimulation of appropriate areas of the cerebral cortex. At birth and during the first days thereafter the hindleg area lay chiefly on the medial aspect of the hemisphere. This and the fact that Weed and Langworthy did not stimulate the facial-masticatory areas on the anteroventral aspect of the hemisphere probably explain their findings. Although responses can be obtained from all parts of the "motor" area at birth, the cortex fatigues quickly and responses cannot be elicited as many times as in older animals. Also with advancing age greater individuation of response occurs, possibly merely because the expanding cortical areas permit the same stimulus to affect a relatively smaller proportion of the face, arm or leg area. [*This work was carried out in 1037-38.*]

Non-production of adiposity in the rat by septal, preoptic and rostral hypothalamic lesions. A. W. HETHERINGTON (introduced by W. F. Windle). *Inst. of Neurology, Northwestern Univ. Medical School, Chicago, Ill.* It has been shown that fairly small bilateral lesions located in the region of the ventromedial hypothalamic nucleus, or at more caudal levels, produce adiposity in the rat (Hetherington and Ranson, 1942). The present work represents an effort to determine whether this is the region really responsible, or whether destruction here causes the syndrome by the severance of fibers from more rostral regions of the hypothalamus or the basal olfactory forebrain.

Bilateral electrolytic lesions of various sizes made with the Horsley-Clarke instrument have been placed in the ventral septal region, the olfactory tubercle, the diagonal band of Broca, the medial and lateral preoptic areas, and the anterior hypothalamic area. In some animals only one of these regions was damaged; in others several in combination were destroyed; and in six the lesions were so large the entire region between the anterior commissure and the rostral edge of the median eminence, between the base and the dorsal limits of the hypothalamus or the anterior commissure, and between the lateral forebrain bundles on each side, was eliminated. In several of this third group the paraventricular nuclei also were destroyed. None of this series of animals became obese.

It is, therefore, assumed that cell groups rostral to the ventromedial hypothalamic nucleus make little if any contribution to regulation of fat metabolism. Whatever the mechanism, it is destruction of the cells in or near that nucleus, or of their descending fibers in the brain stem, which causes the syndrome.

Effect of age on cerebral arterio-venous oxygen difference. HAROLD E. HIMWICH and JOSEPH F. FAZEKAS. *Dept. of Physiology and Pharmacology, Albany Medical College, Union Univ., Albany, N. Y.* Previous work has revealed an average of 6.7 volumes per cent for normal adults from 20

years of age to the late senium. In the present investigation the cerebral arterio-venous oxygen differences were determined on babies less than 2 weeks of age and on undifferentiated mental defectives, i.e., individuals apparently normal except for low intelligence between the ages of 6 and 55 years. The average for the cerebral arteriovenous oxygen difference in 12 observations of the newborn is 8.6 volumes per cent. For the undifferentiated mental defective the average cerebral arterio-venous oxygen difference is lowest from 6 to 9 years of age (30 observations), 4.7 volumes per cent and then gradually rises to 5.1 volumes per cent from 10 to 14 years (33 observations); 5.9 volumes per cent from 15 to 19 years (22 observations); and 6.6 volumes per cent from 20 to 29 years (21 observations). The average cerebral arterio-venous oxygen difference remains unchanged, 6.6 volumes per cent, from 30 to 55 years (24 observations). It is suggested that human brain metabolism, despite the initial large cerebral arterio-venous oxygen difference, is lowest in early life and gradually rises to a maximum between the ages of 20 and 29 years. This maximum is followed by a decrease in the senium.

The effect of sodium 5,5-diphenyl hydantoinate (Dilantin Sodium) upon the tolerance of white rats to low atmospheric pressures. EBBE C. HOFF and CHARLOTTE YAHN (by invitation). *Laby. of Physiology, Yale Univ. School of Medicine, New Haven, Conn. and Physiology Laby., Sarah Lawrence College, Bronxville, N. Y.* The effect of sodium 5,5-diphenyl hydantoinate upon the capacity of white rats to withstand reduced pressures was investigated in 118 animals. In a first series, rats were decompressed at a uniform rate of 100 mm. Hg per minute to the point of apnea both in control "flights" and after subcutaneous injection of a dilantin suspension (1.0 to 4.5 grains). Twenty-eight animals died during control decompression (average "ceiling", 42.1 mm. Hg). Twenty-five animals surviving both control and drug "flights" attained control "ceilings" from 55.3 to 16.9 mm. Hg (average, 35.0 mm. Hg), while after dilantin they withstood pressures from 37.0 to 4.9 mm. Hg (average, 18.6 mm. Hg). In all cases, animals tolerated lower pressures with the drug than without and "ceilings" successfully reached by drugged animals were, generally, higher than those achieved by rats succumbing to control decompression. Dilantin has a relatively greater effect in raising the tolerance of animals with a lower control "ceiling" than those with a greater initial resistance to rarefied atmospheres.

In a second series, rats were decompressed at the standard rate to 70 mm. Hg and maintained at this pressure until breathing ceased. Eighteen control rats were all dead after an average exposure of 1 min. 30 sec., the longest time for a lethal effect being 1 min. 45 sec. Eighteen dilantinized animals similarly decompressed survived from 3 min. 8 sec. to 10 min. 55 sec., in every instance longer than any in the control group.

Relation between androgen output and urinary volume. FRANKLIN HOLLANDER, BRUNO KRISS (by invitation), EMANUEL KLEMPNER (by invitation) and ROBERT T. FRANK (by invitation). *Laboratories of The Mount Sinai Hospital, New York City.* Urinary volume and content of biologically active androgens were studied in 9 humans with normal kidney function, by collecting a continuous series of 3-day specimens for approximately one month. In 3 of the cases, extensive variations in fluid intake were employed to increase the range of urinary output values. Androgen content was assayed by our chick-comb method, previously described; results were calculated in terms both of concentration (dmg. per liter) and total daily output (dmg. per day).

In each subject, the androgen concentration values were constant within the limits of reliability of the assay procedure (standard deviation never greater than 16.5 per cent of the mean), and therefore independent of the daily volume of urine. When expressed as daily output, however, the androgen data were always more variable than in concentration terms; for any one subject, the ratio of the standard deviations (in percent) was 4.5 at the greatest. Furthermore, the variations in daily output of androgens were not random, but were correlated with the urinary volume; the correlation coefficient was never less than 0.72, and for 5 subjects it was 0.95 to 0.99. This is contrary to Oesting and Webster (colorimetric determination). Such constancy of urinary concentration is not in accord with the known behavior of other urinary constituents, and further investigation of this problem from various angles is essential before any conclusions may be drawn regarding its implications. [*Supported in part by a grant from The Friedsam Foundation.*]

The pH of mucus from the gastric corpus. FRANKLIN HOLLANDER and JULIUS STEIN (by invitation). *Laboratories of The Mount Sinai Hospital, New York City.* More than 400 non-acid specimens of mucus were collected from dog's greater curvature pouches in response to the following mechanical and chemical stimuli: gentle rubbing of empty pouch with a smooth catheter, distilled water, aqueous solutions of ethyl ether (saturated), clove oil (5 per cent), mustard oil (1 per cent), ethyl alcohol (50 and ca. 80 per cent), NaCl (0.17 N and 0.5 N). Viscosity of secretion varied extensively, even with any one stimulus. Duplicate pH determinations on the same specimen usually agreed to ± 0.02 pH; our previous failure to obtain such agreement was found to result from the heterogeneity of the specimens, and was

overcome by homogenization. The pH values ranged between 9.07 and 6.00; occasional values below pH 6 were discarded. Their frequency distribution possesses 2 peaks, around 8.0 and 7.1 respectively (although bimodality could not be proved), which suggests that we are probably dealing with a mixture of two fluids of different pH. The lower values result from a predominance of transudate or exudate in the specimens; this is supported by their microscopic appearance. The upper values result from the predominance of a secretory product (mucus and possibly mucoid secretion), since inflammatory exudates rarely attain a pH greater than 7.5.

The data were grouped according to individual stimuli and averaged. The 9 means varied from 7.89 (clove oil) to 7.03 (water); in many cases the difference between any two means was statistically significant, and in others it might become so with increase in frequency. The results indicate that some of these agents are good mucus stimuli whereas others merely induce transudation or exudation. Correlation of pH with buffer capacity, chloride concentration, and microscopic appearance will be reported on elsewhere. [*Supported in part by grants from the United Hospital Fund and John Wyeth and Brother, Inc.*]

Effect of anoxia and hypoglycemia on survival period of adult rats. EDMUND HOMBURGER and HAROLD E. HIMWICH. *Dept. of Physiology and Pharmacology, Albany Medical College, Union Univ., Albany, N. Y.* In order to study the interrelationship between hypoglycemia and anoxia adult male rats were exposed to an atmosphere of 4.5 per cent to 5 per cent oxygen. These adult animals survived on an average for 27 minutes. When in addition to anoxia the animals received insulin one hour before exposure the survival was shortened to 15 minutes while the injection of glucose before subjecting the insulinized animals to anoxia restored the duration of the survival to 28 minutes. It was not possible to prolong the survival of adult rats beyond that period by raising the level of blood sugar above normal. When two groups of adult animals, one fasted and one fed, were subjected to anoxia it was found that the fasted animals suffered a fall in blood sugar and the fed, a hyperglycemia. Despite this difference, the survival period of both groups was the same. This is in agreement with the observations that the hyperglycemia does not prolong the survival of the adult in anoxia.

A method for the production of shock in rats. DWIGHT J. INGLE. *Research Laboratories, The Upjohn Company, Kalamazoo, Mich.* The method of limb ligation which has been widely used for the production of experimental shock has been standardized for the rat.

Male rats of the Sprague-Dawley strain (185-195 grams) are used. The rat is anesthetized by the intra-peritoneal injection of 18 mgm. of cyclopal sodium. The posterior half of the body is shaved. A ligature of strong linen thread is placed about each hind leg and held in place by four short stitches through the skin at the following points: 1, in front of penis; 2, umbilical scar; 3, dorsal side, over the vertebral notch formed by junction of the lumbar and thoracic vertebrae; and 4, just over the first caudal vertebrae. The ligatures are tightened alternately until they are as tight as possible. Second ligatures are then placed in the same positions but are not stitched through the skin. The ligatures are removed after two and one-half hours. By this time recovery from the anesthetic has begun. Food and water are withheld. The incidence of survival for 24 hours is the criterion used to judge the therapy tested. Actual survival time is a more desirable criterion.

In our experiments control groups of 20 untreated rats each are used. In a series of 10 experiments the incidence of survival among control animals has been 25–50 per cent.

The effect of insulin on some metabolic changes induced by 17-hydroxycorticosterone and 17-hydroxy-11-dehydrocorticosterone in the rat. DWIGHT J. INGLE, GORDON B. GINTHER (by invitation), JOHN S. EVANS (by invitation), ARNE N. WICK (by invitation) and MARVIN H. KUIZENGA (by invitation). *Research Laboratories, The Upjohn Company, Kalamazoo, Mich.* The administration of 5 mgm. daily of either 17-hydroxycorticosterone or 17-hydroxy-11-dehydrocorticosterone to normal, force-fed rats causes the development of a diabetic state characterized by glycosuria, hyperglycemia, increased excretion of N.P.N., a marked loss of weight and changes in electrolyte balance. The amount of urinary glucose cannot be accounted for on the basis of increased protein catabolism. Such animals are abnormally resistant to insulin. In animals showing mild glycosuria it was possible to control the diabetic state by the administration of large doses of protamine zinc insulin but these animals continued to excrete greater than normal amounts of N.P.N. and they failed to gain weight. In some animals having a severe glycosuria it was not possible to completely control the excretion of glucose by means of insulin. When the administration of the adrenal steroids was stopped the glycosuria disappeared.

The diabetogenic effect of diethyl-stilbestrol in adrenalectomized-hypophysectomized-partially depancreatized rats. DWIGHT J. INGLE and GORDON B. GINTHER (by invitation). *Research Laboratories, The Upjohn Company, Kalamazoo, Mich.* The diabetogenic effect of diethyl-stilbestrol occurs in partially depancreatized and normal rats (Endocrinology 29: 838, 1941) and in partially depancreatized-adrenalectomized rats treated with

sub-diabetogenic amounts of adrenal cortical extracts (Am. J. Physiol. in press). To test the hypothesis that the diabetogenic activity of diethyl-stilbestrol may be mediated through the anterior pituitary or the adrenal and pituitary glands together, adrenalectomized-hypophysectomized-partially depancreatized male rats were used as test animals. In experiment 1, the animals were maintained on sub-diabetogenic amounts of adrenal cortical and anterior pituitary extracts. The administration of diethyl-stilbestrol caused glycosuria and hyperglycemia in each animal. In experiment 2, a nearly total pancreatectomy was performed so that all of the animals exhibited spontaneous glycosuria when treated with adrenal cortex and anterior pituitary extracts. In those cases where the glycosuria was mild it became severe on administration of diethyl-stilbestrol, however, when the spontaneous glycosuria was severe the administration of diethyl-stilbestrol failed to intensify it. Although it was clearly demonstrated that diethyl-stilbestrol has some diabetogenic effect which is not mediated by either the adrenal or pituitary glands, its action was less marked than in animals having these two glands intact.

The quantitative assay of adrenal cortical hormones by the muscle-work test in the adrenalectomized, nephrectomized rat. DWIGHT J. INGLE. *Research Laboratories, The Upjohn Company, Kalamazoo, Mich.* Male rats (180 grams) of the Sprague-Dawley strain were used. The diet was Purina dog chow. A standard dose of luminal sodium and of cyclopal sodium is used for anesthesia. The adrenals and kidneys are removed in a single stage operation. Temperature is constant at 28°C. The left gastrocnemius muscle is weighted with 100 grams and stimulated to contract three times per second until "fatigued" or for 24 hours. The distance the weight is lifted is recorded automatically. The test substance is administered in 0.5 cc. of sesame oil at the beginning of stimulation and again 6 hours later. A dose-response curve was set up for 17-hydroxy-11-dehydrocorticosterone. Doses of 0.16 mgm., 0.20 mgm., and 0.25 mgm. of this substance were tested in a large number of animals to provide data for statistical analysis and for a standard dose-response curve which would permit the interpolation of work performance into units of the standard. One unit is defined as the work equivalent of two 0.2 mgm. doses of 17-hydroxy-11-dehydrocorticosterone. The relative error for assay is less than 25 per cent when an average value for work of 15 or more rats falls within the range of the standard dose-response curve.

Response of rats to diethylstilbestrol following thyroidectomy. R. G. JANES (introduced by W. O. Nelson). *Dept. of Anatomy, Wayne Univ. College of Medicine, Detroit, Mich.* Twenty-one female rats were thyroidectomized, in some cases 8 months and in others 10 days before the experiment began. Twelve of these animals, some from each group, were given daily subcutaneous injections of 100 micrograms of diethylstilbestrol for 20 days.

The averages for body weight, blood glucose levels, muscle glycogen and total N.P.N. were similar in control and injected rats. The liver glycogen values, however, were increased from 122 mgm. per cent to 488 mgm. per cent in animals which received diethylstilbestrol. The latter value is higher than was previously reported for unoperated animals which received treatment with estrogens.

The adrenals were reduced in size following thyroidectomy and diethylstilbestrol only slightly increased this size. Following fixation in osmic acid, lipoid was quite evenly dispersed throughout the cortex of controls, but was largely confined to the glomerulosa in the injected animals. The pituitaries were larger following thyroidectomy and microscopically showed an increase in number and vacuolization of the basophils. The weight of the pituitaries increased further after diethylstilbestrol treatment and the vacuolization of the basophils tended to disappear. In fact, the amount of liver glycogen, in general, could be correlated with the condition of the basophils. Those in which the vacuolization was largely corrected had the highest liver glycogen.

Antirenin. C. A. JOHNSON (by invitation), E. L. SMITH (by invitation), BERNARD GOMBERG (by invitation) and G. E. WAKERLIN. *Depts. of Physiological Chemistry and Physiology, Univ. of Illinois College of Medicine, Chicago.* We have used the term antirenin to designate the antibody (antihormone, antienzyme) formed when heterologous renal cortical extracts containing renin are injected into various species of animals. Antirenin is demonstrated in the serums (or plasmas) of the treated animals by its ability to neutralize the acute pressor effect of renin.

Fourteen renal hypertensive, two spontaneously hypertensive and four normotensive dogs were given daily intramuscular injections of hog renin for 3 to 6 months. Three normotensive dogs were similarly injected with rabbit renin. Antirenin developed in all of these animals in 40 to 60 days with extremes of 14 and 164 and disappeared in 30 to 160 days after the injections were stopped. A second course of hog renin in five of the animals resulted in the reappearance of antirenin in 10 to 20 days. Antirenin failed to develop in five hypertensive and four normotensive dogs injected with heat-inactivated hog renin, in six hypertensive and four normotensive dogs injected with dog renin, and two hypertensive and four normotensive

dogs injected with liver extract prepared after the manner of renin.

Antirenin was produced in rabbits and guinea pigs by hog, dog and cat renins. Human renin but not rabbit renin produced antirenin in rabbits.

Serums of dogs injected with hog renin neutralized the acute pressor effect of hog, dog, rabbit and cat renins but not human and rat renins. Antirenins produced by various renins in the rabbit likewise showed considerable crossing of neutralizing properties except human antirenin which appears specific for human renin.

Calculation of enzyme-inhibitor equilibrium constants in relation to changes in optimum temperatures. FRANK H. JOHNSON and HENRY B. EYRING (by invitation). *Dept. of Biology and Chemistry, Princeton Univ., Princeton, N. J.* Inhibitors which enter into an equilibrium K_2 with an enzyme independently of the reversible heat

$$K_1 \left(= e^{-\frac{\Delta H_1}{RT}} e^{\frac{\Delta S_1}{R}}\right)$$

denaturation shift the optimum to a higher temperature. The constant K_2 may be arrived at from the following expression, in which I_1 and I_2 represent the rates of the uninhibited and the inhibited reaction, respectively, X the molar concentration of inhibitor, and r the number of molecules of X combining with one molecule of enzyme:

$$\left(\frac{I_1}{I_2} - 1\right) = K_2 X^r.$$

The changing optimum temperature is given by the point of intersection of y and z, where

$$y = 1 - \frac{\Delta H_1}{\Delta H^\ddagger + RT} \cdot \frac{K_1}{1 + K_1}$$

and

$$z = \frac{\Delta H_2}{\Delta H^\ddagger + RT} \cdot \frac{K_2 X^r}{1 + K_2 X^r} = \frac{\Delta H_2}{\Delta H^\ddagger + RT} \cdot \frac{I_1 - I_2}{I_1}.$$

In these expressions, $\Delta H\ddagger$ represents the energy of activation, while ΔH represents the heat of reaction and ΔS the entropy in the equilibrium designated by subscript number.

Inhibitors which combine with an enzyme in a manner (K_3) that promotes the reversible denaturation, shift the optimum to a lower temperature. The constant

$$K_3 \left(= e^{-\frac{\Delta H_3}{RT}} e^{\frac{\Delta S_3}{R}}\right)$$

may be obtained from the following:

$$\left(\frac{I_1}{I_2} - 1\right)\left(1 + \frac{1}{K_1}\right) = K_3 X^r.$$

The expressions for y and z in this case are,

$$y = 1 + \left(1 - \frac{\Delta H_1}{\Delta H^\ddagger + RT}\right) K_1,$$

and

$$z = \left(\frac{\Delta H_1 + \Delta H_3}{\Delta H^\ddagger + RT} - 1\right)$$

$$(K_1 K_3 X^r) = \left(\frac{\Delta H_1 + \Delta H_3}{\Delta H^\ddagger + RT} - 1\right)\left(\frac{I_1 - I_2}{I_2}\right)(1 + K_1),$$

in which the notation has the same meaning as before. In luminescence, sulfanilamide exemplifies the former, and urethane the latter of the above types of inhibition.

The response of hypophysectomized rats to intraperitoneal glucose injections. SAMUEL JOSEPH (by invitation), MALVINA SCHWEIZER (by invitation) and ROBERT GAUNT. *Dept. of Biology, Washington Square College of Arts and Science, New York Univ.* The effects of intraperitoneal injections of isotonic glucose solution were studied in normal, hypophysectomized and adrenalectomized male rats, in order to analyze the nature and cause of the abnormal response of hypophysectomized animals to this treatment (Gaunt, Remington and Schweizer, 1937). Measurements indicated below were made at 3, 6 and 12 hour intervals in 84 normal, 78 hypophysectomized and 8 adrenalectomized animals.

Hypophysectomized rats resembled intact ones in respect to (1) the initial transfer of fluid, electrolyte, and protein to the peritoneal cavity, and (2), if the animals were not moribund, in their subsequent absorption of fluid, electrolyte, protein, and glucose from the peritoneal cavity.

Hypophysectomized animals differed from normal animals in these respects: 1, hemoconcentration was more severe; 2, there was little or no hemodilution as ascitic fluid was absorbed; 3, blood pressure and body temperature declined to lower levels; 4, stasis occurred in the peripheral circulation (web of foot); 5, little urine excretion occurred, and 6, many animals succumbed.

All major deficiencies and death were prevented in hypophysectomized animals by the administration of adrenal cortical hormones, and therefore presumably were of adrenal origin.

Hypophysectomized animals, while resembling adrenalectomized ones in their susceptibility to the shock-like circulatory failure, did not show similar shifts in water and electrolyte. This difference was exemplified by the fact that adrenalectomized rats transferred much smaller amounts of water and electrolyte to the peritoneal cavity in the early post-injection stages than either intact or hypophysectomized animals.

Bile effect on gastric motility after histamine injections. JERZY KAULBERSZ (introduced by T. L. Patterson). *Wayne Univ., College of Medicine.* Previous studies indicated that bile introduced into a fasting dog's stomach during the quiescent phase stimulates gastric motility. If

the resting phase is not physiologically produced but pharmacologically provoked by atropine, bile is without effect. Since secretion of gastric juice or bringing in of free acid into the stomach inhibits gastric hunger contractions, it was of interest to establish how bile would act during the quiescent phase following histamine injection.

Histamine given subcutaneously decreases after 15–30 minutes gastric hunger contractions and then provokes a more or less complete resting phase lasting for about 1 hour. Usually in 75–90 minutes following histamine injection the hunger contractions are resumed. Bile introduced directly into the fasting, fistularized dog's stomach during this resting phase called forth contractions of short duration in only 3 of 22 experiments, while in the *majority of cases no influence was noted. Thus,* it seems that the normal spontaneous resting phase between gastric hunger contractions has some other physiological properties than that provoked by histamine.

Histamine injected during the period of digestive contractions after beef heart intake did not call forth a resting phase, but bile introduced thereafter into the stomach inhibited slightly the contractions and decreased the tone. Weak contractions following the feeding of canned dog food are diminished by histamine but there is no further effect produced by bile.

Reaction of the human stomach and intestine to bile. JERZY KAULBERSZ and JAMES M. WINFIELD (introduced by T. L. Patterson). *Wayne Univ., College of Medicine.* Direct registration and introduction of bile into gastric and intestinal fistula patients as well as a double tube with a balloon brought in through the nose or mouth were employed.

Bile introduced during the resting phase of a fasting human stomach did not stimulate the motility in 16 of 20 experiments, which is contrary to that obtained from dog's stomach. In 4 experiments some isolated contractions were observed and slight changes in tone. Bile salts and potassium which exert the same effect as whole bile in a fasting dog's stomach, are also without influence on the human stomach. However, we could confirm the observations of some investigators that under the action of bile there is a decrease in emptying time of the stomach.

Registration of bile effect on the motility of jejunum did not reveal a stimulation, but a slight inhibition occurred during the contractions. The motility stimulating action of bile was only noted on the human ileum. In 10 experiments carried out on 2 patients, one with an ileum fistula, the other with an incisional hernia, bile and bile acids introduced during the resting phase produced immediately strong intestinal contractions lasting for several minutes.

These observations reveal an analogy in the response to bile of human ileum and dog's stomach, while from work of other investigators the positive action of bile on dog's intestine may be included. The human stomach has a more stable resting phase; it seems to be a more powerful peacemaker than the dog's stomach.

Electroencephalograms of decorticate monkeys. MARGARET A. KENNARD. *Laby. of Physiology, Yale Univ., New Haven, Conn.* Rhythmic potential variations were obtained from nuclear areas at the base of the brain after complete decortication in the monkey under dial narcosis.

1. *Basal ganglia.* Potentials obtained from caudate and putamen are characterized by spontaneous bursts appearing often only once or twice *a minute, at other times every two or three seconds.* They varied from 8 to 15 per second and from low amplitude at the beginning and end to very high in the middle of each burst. Potentials recorded from caudate and putamen of one side were always alike in shape and timing. Those from the two sides showed no temporal relation except that both sides had simultaneous times of great activity followed by intervals of much less activity.

2. *Thalamus.* The thalamus produced potential changes which were faster than those of basal ganglia and more like those of cortex. They varied slightly in pattern and amplitude but were constantly present and not subject to spasmodic bursts.

3. *Hypothalamus.* From the hypothalamus very slight activity occurred which was of low amplitude, constant and regular at a rate of about ten per second.

These potential characteristics of the different nuclear groups appeared distinct only when all of the cerebral cortex had been removed from both hemispheres. In the presence of cortex the same areas produced only cortical types of potentials although with slight regional differences. No spontaneous bursts of activity appeared on the record until all of cortex had been removed.

A metabolite of brain which reacts with *p*-aminobenzoic acid, the sulfonamides, and other aryl amines. HENRY I. KOHN. *Dept. of Physiology and Pharmacology, Duke Univ. School of Medicine, Durham, N. C.* When brain brei (rat, rabbit, guinea pig) is suspended in Ringer-phosphate and incubated at 38°, a substance *B* is produced which reacts to form a pigment with *p*-aminobenzoic acid, the sulfonamides, and other substituted aryl amines. The reaction is most rapid in acid solution, but can also occur slowly at pH 7.4. The stability of the pigment is greatest in acid solution.

The production of *B* presumably involves enzymatic processes and is coupled with the respiration.

No *B* is formed, for example, in the presence of 5 per cent trichloracetic acid or of 25 per cent alcohol. If old brain (stored in the cold for 6 hours) instead of fresh brain is used, the production of *B* is impaired. No *B* is produced under anaerobic conditions.

These data suggest that the toxicity of the sulfonamides for man may be explained in part by their interference with the metabolism of *B*. Furthermore, they provide what may prove to be a chemical model of the bacterial reaction in which it has been postulated that *p*-aminobenzoic acid and sulfonamide compete for a compound not yet specified.

The excretion of calcium by the colon of the unanesthetized dog. A. J. KOSMAN (by invitation) and SMITH FREEMAN. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* The effect of mildly irritating mustard oil-saline solutions upon the excretion of calcium by chronic colon fistulae was studied in three dogs. The following procedure was carried out: the colon loop was washed thoroughly with warm isotonic saline and samples of the final washing saved for calcium determinations. The fistula was then perfused with 500 cc. of warm isotonic saline by means of a constant injection pump which circulated the fluid about 6 times an hour. At the end of one hour the irrigation was discontinued and the saline irrigate collected.

A second perfusate of 500 cc. isotonic saline + 6 drops of mustard oil was then circulated through the fistula for one hour. The perfusates were dried and ashed and total calcium determined. The averaged results of 26 experiments were: Saline perfusate; total calcium, 7.4 mgm. (range 2.7–11.6); mustard oil perfusate; total calcium, 13.9 mgm. (range, 6.7–24.4).

Similar experiments were carried out on two dogs with chronic jejunal fistulae. The averaged results of ten experiments were: saline perfusate; total calcium, 1.24 mgm. (range 0.9–2.3 mgm.); mustard oil perfusate: total calcium, 4.7 (range 1.7–8.8).

In a third group of experiments, the colon fistula of one dog was perfused for one hour with 500 cc. of isotonic saline; the perfusate was then collected and the animal given 2 mgm. pilocarpine subcutaneously. A second perfusate of isotonic saline was then circulated for one hour. The averaged results of eight experiments were: Saline perfusate: total calcium, 5.9 mgm. (4.8–6.7); pilocarpine: total calcium, 13.5 mgm. (8.9–16.1).

In no instance did the irritant or the drug fail to produce an increase in the total calcium of the perfusate. Further experimentation correlating mucin secretion with calcium excretion by the colon are in progress.

Spermatozoa content of the seminal vesicles of *Macaca mulatta*. JULE K. LAMAR (*now at the Department of Obstetrics and Gynecology, the University of Texas Medical Branch, Galveston*), (introduced by Carl G. Hartman). *Carnegie Laby. of Embryology, Baltimore.* Six adult rhesus monkeys, used formerly for breeding and experiment, were investigated 10 minutes to 3 hours (less than 15 min. in 4 cases) after death. Five were killed by air embolism, and one died. All were in poor health. The seminal vesicles were enucleated carefully, then the vasa deferentia.

Sperm content of seminal vesicles was 0 to 118 millions/cc. (average, 5.9 millions/cc.). Sperm content of the vasa was 3 hundred to 16.3 billions/cc. (average, 3.55 billions per cc.). In those seminal vesicles containing spermatozoa, motility averaged 19 per cent low grade motion in place. In the vasa deferentia, motility averaged 48 per cent good grade forward motion. Vesicle spermatozoa were 70 per cent grossly abnormal in shape, whereas spermatozoa in the vasa deferentia showed less than 20 per cent abnormal forms.

Because the semen of the rhesus monkey generally contains about one billion spermatozoa per cc. in the fluid portion, these data suggest that: 1, in this species the seminal vesicles do not act as sperm storage organs, and 2, the relatively few spermatozoa which can be found there from time to time are not physiologically or morphologically normal.

Increase of the renal filtration fraction after plasmapheresis. HAROLD LAMPORT, ESTHER MACULLA and SAMUEL GRAFF (introduced by J. F. Fulton). *Laby. of Physiology, Yale Univ., New Haven, Conn., and Depts. of Pharmacology, of Obstetrics and Gynecology, and of Biochemistry, Columbia Univ., New York City.* On the basis of the principle of homeostasis, it was previously concluded that reduced serum protein should give rise to an increase in the renal filtration fraction (J. Clin. Invest. 21: 685, 1942). Since the fraction has been found reduced rather than increased in severe toxemia of pregnancy, where the serum protein is low, the experimental verification of this conclusion in the intact organism becomes important.

Seven female dogs under pentobarbital anesthesia were subjected to plasmapheresis, renal blood flow and glomerular filtration rate being measured by diodrast and inulin clearances. In six of the seven experiments, the filtration fraction rose when serum protein fell. The statistical likelihood that this finding is significant is 94%.

In two of three control experiments involving return of the drawn heparinized blood without resuspension of the cells, a slight fall in filtration fraction was found. Pentobarbital alone on two successive days did not affect the filtration fraction. These controls indicate that the rise in fil-

tration fraction was correlated with the fall in serum proteins.

The action of some phenylethyl amines on the intestine and heart. A. M. LANDS and C. W. GEITER (by invitation). *Frederick Stearns and Company, and Wayne Medical College, Detroit.* The hydrochlorides of the compounds listed below have been investigated for their action on the isolated rabbit jejunum (Magnus method) and some of them for their action on the isolated tortoise auricle and the perfused frog heart. In the perfusion experiments all injections were made directly into the perfusion stream near the heart and the drug washed out of the tissue by the Ringer solution flowing through the organ.

Isolated segments of the rabbit jejunum were relaxed by allyl-beta-phenylethyl amine (II), in a dilution of 1:20,000; by dibutyl-beta-phenylethyl amine (IV), methyldi-beta-phenylethyl amine (V), ethyldi-beta-phenylethyl amine (VI) in 1:400,000 to 1:200,000; by propyldi-beta-phenylethyl amine (VII) in 1:1,000,000 to 1:400,000. Ethyl-beta-phenylethyl amine (I), diethyl-beta-phenylethyl amine (III), and tri-beta-phenylethyl amine (VIII) were without action in dilutions of 1:10,000. However, ethyl-beta-phenylethyl amine injected intravenously into anesthetized dogs and rabbits in amounts of 0.1–0.5 mgm./kgm. caused relaxation of the intact jejunum associated with a rise in blood pressure. The duration and intensity of the relaxation corresponded closely with the changes in blood pressure.

Compounds I, II, III and V in 1–4 mgm. doses slow the rate of contraction of the perfused frog heart and cause some reduction in the amplitude of beat. Compound VI depresses cardiac activity; doses of 0.1–0.5 mgm. arrest all contraction in diastole. At least one half hour in Ringer solution is required to restore rhythmic contraction. Compound I in 1:20,000 causes a reduction in the amplitude with some increase in the rate of contraction of the isolated tortoise auricle. In this dilution, there is complete inhibition of the tonus waves that these preparations sometimes show. With a dilution of 1:4,000 there is a reduction in both rate and amplitude. Similar observations were made for compounds II, III, and V. Other compounds in this series were not used on the auricle.

The activity of the adrenal cortex of rats exposed continuously to low atmospheric pressure. L. L. LANGLEY (introduced by J. F. Fulton). *Laby. of Physiology, Yale Univ. School of Medicine, New Haven, Conn.* It has been reported (Langley and Clark. Yale J. Biol. Med. 14: 529, 1942) that adrenalectomized rats require more adrenal cortical hormone for survival while exposed to a simulated altitude of 20,000 feet than adrenalectomized rats living at sea-level. It was found, however, that after a few days exposure, the amount of hormone required diminished so that ultimately the requirements of the exposed group were the same as that of the controls. It seemed of interest to determine whether an intact animal exposed to anoxia for 6 days, and then adrenalectomized would, nevertheless, require increased amounts of the extract, or whether the adapted animals could survive with only the amount required by the sea-level controls. The experiments previously reported indicated that the latter alternative would be correct.

Rats were exposed continuously at an altitude of 20,000 feet. After the usual drop in body weight all of the animals showed a progressive gain. After 6 days the loss of weight had been regained. At this time they were adrenalectomized at sea-level, and returned to the decompression chambers. Each morning they were injected with 0.5 cc. of cortical extract. They all survived and gained weight comparable to that observed in intact animals. Rats that had not previously been exposed were adrenalectomized at the same time, and subjected to the identical treatment. These steadily lost weight, and after a few days died. Thus, the conclusion that exposure of rats to 20,000 feet altitude causes an activation of the adrenal cortex, which, after a few days, returns to normal, is confirmed.

Metabolism of radioactive iodine in the thyroids of rats kept at low temperature. C. P. LEBLOND, J. GROSS, W. C. PEACOCK and R. D. EVANS (introduced by Hans Selye). *Dept. of Anatomy, McGill Univ., Montreal, P.Q. and Dept. of Physics, Massachusetts Inst. of Technology, Boston.* The metabolism of radioactive iodine in the thyroid glands was examined after the injection of 5 micrograms of radioactive iodide to adult rats kept at 0°C for 1, 3, 7 or 26 days.

A significant increase in the amount of iodine fixed two hours after injection was found only in the thyroids of those animals which had been kept in the cold for 7 or more days. The increase in the iodine uptake of the thyroid was moderate in the seven-day group and very marked in the 26-day group being at least three times the amount fixed by the controls kept at room temperature. Similarly, histological examination after a seven-day exposure to cold showed signs of clear cut thyroid stimulation in most of the animals, while after twenty-six days at 0°C the activation of the thyroid appeared intense. Measurement of the radioactivity in the inorganic iodide, diiodotyrosine and thyroxine fractions of the gland showed an increased turnover and excretion of iodine with more rapid formation of thyroxine in the 7- and especially the 26-day group.

These results indicate that exposure of adult rats to cold causes an increase in thyroid activity. This response is comparatively slow at 0°C, becom-

ing clearly observable at seven days and rising to 3 times the normal level at 26 days.

Iodine metabolism in the thyroid gland after single injections of 5 or 500 micrograms of radioactive iodine to adult rats. C. P. LEBLOND, W. C. PEACOCK, J. GROSS, and R. D. EVANS (introduced by H. Selye). *Dept. of Anatomy, McGill Univ., Montreal, and Dept. of Physics, Massachusetts Inst. of Technoloyy, Boston.* After single intravenous injections of 5 or 500 micrograms of radio-iodine to adult rats, the distribution of radio-iodine in the inorganic iodide, diiodotyrosine and thyroxine fractions of the thyroid was determined at intervals of 15 minutes, 2 and 30 hours after injection.

The uptake of iodine by the thyroid in the case of the smallest dose was progressive, increasing markedly with time, while with the larger dose there was only a relatively slight increase with time.

Fractionation of the thyroid showed that after 15 minutes or two hours most of the radio-iodine was present as inorganic iodide, while after 30 hours the radioactivity predominated in the diiodotyrosine fractions. This distribution was comparable for the two dosages.

A comparison of the percentage of radioactivity in each thyroid fraction with that of the total gland at the various time intervals indicate that in the dosages used, iodine entering the thyroid does so as inorganic iodine and is fairly rapidly converted into diiodotyrosine.

The antispasmodic action of some para-xenyl acetic acid esters. J. R. LEWIS (by invitation), A. M. LANDS and C. W. GEITER (by invitation). *Frederick Stearns and Company, and Wayne Medical College, Detroit.* The antispasmodic action of the hydrochlorides of several derivatives of the biphenyl compounds, b-diethylaminoethyl-p-xenyl acetate, b-piperidinoethyl-p-xenyl acetate, y-diethylaminopropyl-p-xenyl acetate and y-piperidinopropyl-p-xenyl acetate, has been determined on the isolated rabbit jejunum according to the technique of Magnus. Compounds with a methyl, ethyl, propyl, phenyl or cyclohexyl substitution on the acetate radical were tried for all the above esters except the last, in which case only the methyl and phenyl substitutions were available. In all instances, the methyl derivatives were the most active. Thus b-diethylaminoethyl-p-xenyl acetate HCl relaxes the unstimulated jejunal segment in 1:100,000–1:200,000 whereas b-diethylaminoethyl-methyl-p-xenyl acetate relaxes in 1:1,000,000–1:2,000,000; b-piperidinoethyl-p-xenyl acetate relaxes in 1:200,000–1:400,000 whereas b-piperidinoethyl-methyl-p-xenyl acetate will relax in 1:2,000,000–1:4,000,000; y-diethylaminopropyl-p-xenyl acetate relaxes in 1:40,000 whereas y-diethylaminopropyl-methyl-p-xenyl acetate relaxes in 1:1,000,000–1:2,000,000. Compound y-piperidinopropyl-methyl-p-xenyl acetate relaxes in 1:500,000–1:1,000,000. Increase in the size of the substituted group to ethyl, propyl, phenyl, or cyclohexyl, resulted in a reduction in antispasmodic activity from that of the methyl compound.

Intravenous injections of b-piperidinoethyl-methyl-p-xenyl acetate were made into anesthetized dogs and rabbits and recordings made of the motility of the intact jejunum. Moderate relaxation was obtained in the rabbit with 0.05–0.1 mgm./kgm. and in the dog with 0.5 mgm./kgm., lasting for about 15 minutes. Intravenous doses of 1.0 mgm./kgm. had no effect on the carotid blood pressure of dogs. The p-xenyl acetates are irritating to the rabbit conjunctiva; with resulting hyperemia and edema and in some instances corneal opacity. The toxicity of the most active compound, b-piperidinoethyl-methyl-p-xenyl acetate, was determined in albino mice by intraperitoneal injection. A dose of 150 mgm./kgm. killed 13 out of 25 mice, most of the deaths occurring within the first few minutes. In general, toxic manifestations were those of central stimulation.

The afferent fibers mediating myotatic reflexes and their central connections. DAVID P. C. LLOYD. *Laboratories of the Rockefeller Inst. for Medical Research, New York City.* The afferent response to sudden, brief stretch applied to M. Gastrocnemius is conducted at 105–115 M/sec., terminates with the cessation of stretch and suffers minimal dispersion by reason of conduction to the spinal cord. Thus the largest, lowest threshold afferent fibers are involved.

Stimulation of the lowest threshold afferent fibers in the gastrocnemius nerves results in the appearance of a two-neuron-arc discharge in the first sacral ventral root. Stimulation of the lowest threshold fibers in the first sacral dorsal root results in two-neuron-arc discharge into the gastrocnemius nerves. However, stimulation of one muscle nerve, while yielding ample two-neuron-arc discharge into the ventral root, does not result in that discharge appearing in any other muscle nerve. There is no reflex from one head of M. Gastrocnemius to the other. Such discharges as are found pertain to multineuron-arc paths, are virtually confined to flexor muscle nerves and occur when cutaneous or high threshold muscle afferent fibers are stimulated. It follows that the two- neuron-arc discharge reflects only into the muscle or fraction of a muscle from which it may be said to arise. The intensely local nature of the two-neuron-arc discharge in contrast to the diffuseness of the multineuron-arc discharges accounts for the intensely local nature of the myotatic reflex (Sherrington).

The evidence points to the conclusion that the most rapidly conducting afferent fibers and the most direct central reflex pathways are reserved for the mediation of myotatic reflex action.

Influence of sulfonamides on neuromuscular responses of rats. DAVID I. MACHT (with technical assistance of Ruth Legg). *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* The psychological effects of sulfonamides being of clinical importance in the war effort, experiments were made on the behavior and neuromuscular responses of rats after injection of sulfanilamide, sulfathiazole and sulfadiazine by studying 1, the behavior of rats in a circular maze to discover their activity as well as learning and discriminatory faculty; 2, the effect of drugs on the neuromuscular coordination of the legs of rats walking a tight rope, and 3, the influence of such injections on their ability to climb a perpendicular rope to determine the working capacity of the skeletal muscles. Twenty adult pedigreed rats were employed in a series of 150 experiments. Doses of drugs injected ranged from 10 to 200 mgm., those below 20 mgm. producing little effect. Twenty to 40 mgm. effected a transient depression with recovery the same afternoon, even after injections on three successive days. Fifty to 100 mgm. produced greater depression, also with rapid recovery. Quantities of 100 to 200 mgm. markedly affected all the test animals. The most depressant of the sulfonamides by far was sulfathiazole, which weakened especially the neuromuscular responses normally exhibited in climbing. The least depressant was sulfadiazine which even in doses below 75 mgm., usually induced excitement and quicker performance. The animals invariably recovered in a few days even after large doses. Note that doses of 30 mgm. for rats of 200 grams' weight equals 150 mgm. per kilogram, corresponding to a dosage of 9 grams for a man of 60 kilograms.

Effect of amino benzoic acids and sulfanilamide on lupinus seedlings. DAVID I. MACHT and DOROTHY B. KEHOE (by invitation). *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* Studies were made by the author's well-known methods on the growth, under standardized conditions (temperature, light, etc.), of *Lupinus albus* seedlings in plant-physiological solutions with and without amino benzoic acids and sulfanilamide, separately and together. Of the three amino benzoic acids the meta-amino variety is the most toxic, the ortho-amino coming next and the para-amino being least toxic, the indices for seedlings grown in 1:20,000 solutions of the three acids for 24 hours at 60°C. in the dark being 31, 50 and 64 per cent, respectively. Para-amino benzoic acid ("Paba") in dilutions of 1:1,000,000 or more stimulated growth; stronger concentrations inhibited it. Seedlings grown in 1:10,000 and 1:25,000 sulfanilamide solutions gave indices of 68 and 73 per cent, respectively. Solutions of sulfanilamide less than 1:200,000 stimulated growth. A combination of Paba and sulfanilamide in various concentrations uniformly exerted a synergistic or more toxic influence on growth of *Lupinus albus* seedlings than could be obtained by adding the effects of the individual constituents. This was true also of seedlings grown in *water* without physiological salts and also held good for excised *Lupinus* roots. The well-known inhibitory action of para-amino benzoic acids for bacteria, trypanosomes and malarial plasmodia and the findings described above strongly suggest that bacteria are more closely related to microscopic animals than to microscopic plants.

Influence of heparin on growth of lupinus albus seedlings. DAVID I. MACHT. *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* In connection with a general study of its pharmacodynamic properties, the effects of heparin were studied on root growth of *Lupinus albus*. Seeds were germinated in ground sphagnum and root growth of seedlings was studied hydroponically under standard ecological conditions (light, temperature, etc.) in Shive solution for 24 hours. The index of growth is expressed by the formula $\frac{N}{X}$, in which N expresses the average root growth of controls and X that of seedlings placed in heparin solutions of the same plant-physiological saline. Growth of seedlings for 24 hours in concentrations of heparin varying from 1:1,000 to 1:100,000 at 15–16°C. in the dark was measured, and a peculiar growth curve was obtained. Some of the concentrations stimulated root growth above normalcy while others inhibited it. Peaks of growth were reached in solutions of 1:100,000, 1:45,000 and 1:20,000, the indices obtained therein being 112, 111 and 113 per cent, respectively. The greatest inhibition occurred in concentrations of 1:65,000, 1:35,000 and 1:1,000. The indices of growth reached in these solutions were 75, 82 and 66 per cent, respectively. Practically identical were the results obtained with samples of Swedish, Swiss, Canadian and American (H. W. & D.) heparin. Heparin is a mucoitin polysulfuric acid. A synthetic analogue, the sodium salt of polyanethol sulfonic acid (*Liquoid* Roche), far from stimulating, exerted a toxic action and inhibited growth in solutions of 1:100,000. Stronger concentrations were even more toxic in direct proportion to the amount of the drug employed.

Action of snake venoms on the intestinal tract. DAVID I. MACHT. *Pharmacological Research Laby.,*

Hynson, Westcott & Dunning, Inc., Baltimore, Md. Normal cats, guinea pigs and rats were parenterally injected with a physiological salt solution of snake venoms in lethal and sublethal doses, as tested by assay on mice; and a difference was noted between *COLUBRIDAE* and *VIPERIDAE* Venoms with regard to their effect on bowel movements and purgation. Venoms of the *COLUBRIDAE—Naja tripudians, Naja naja, Hamadryas* (king cobra), *Bungarus fasciatus* (krait), and *Sepedon haemachates*—rarely exerted a purgative action. Venoms of the *VIPERIDAE —Daboia* (Russell's viper), *Bothrops atrox, Lachesis gramineus* and *Agkistrodon piscivorus* and several species of *Crotalus*—usually effected purgation, and *Daboia* venom produced bloody stools. Experiments on rats by the Macht-Barba-Gose method (J. A. Ph. A., 20: 558, 1931) revealed that these venoms did not stimulate intestinal peristalsis directly but inhibited it. The purgative action of *VIPERIDAE* venoms appears there to be due to general poisoning rather than to selective stimulation of the intestines. Cobra venom increased the tonicity of isolated intestinal loops of cats and rabbits in vitro as did *Daboia* and *Crotalus* venoms although not so much as cobra venom. Treatment of such loops from 5 to 15 minutes with venom did not paralyze their response to epinephrine, pilocarpine, atropine, etc. Results of these experiments with intact animals are comparable to symptoms of snakebite in man as described by Noguchi, Prentice Willson and others. In reports of thousands of clinical cases treated therapeutically with cobra venom solution (H. W. & D.) no laxative or purgative effect was noted.

The toxicity of snake venoms after administration by stomach. David I. Macht and Dorothy B. Kehoe (by invitation). *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* Numerous experiments were made by comparing the toxicity of snake venoms after parenteral injection with their toxicity after administration by special stomach tube to mice. Contrary to the belief held by laymen and many physicians, adequate doses of most snake venoms are toxic when given orally. A great difference in toxicity, however, was noted between the venoms of the *COLUBRIDAE* and those of the *VIPERIDAE*. The *COLUBRIDAE* venoms studied were the *Naja naja, Naja tripudians, Naja haji, Naja nivea, Hamadryas* (king cobra), *Bungarus fasciatus* (krait), *Sepedon haemachates* and *Micrurus fulvius*. The *VIPERIDAE* venoms studied were the *Daboia* (Russell's viper), *Bothrops atrox, Lachesis gramineus, Agkistrodon piscivorus, Agkistrodon mokasen, Bitis arietans* and eighteen species of *Crotalus*. The *COLUBRIDAE* venoms, rich in neurotoxin, are lethal for mice when given by stomach in doses of 0.5 to 2.0 mgm. Of all the *VIPERIDAE* venoms studied at least 20 mgm. were required to kill when administered to mice by stomach. The venoms of rattlesnakes had a wide range of toxicity, some proving fatal in doses of 30 mgm. and others having a lethal dose of over 100 mgm. when administered by stomach to mice. Results of biochemical studies on neurotoxins of several venoms of each group by Van Eswald's method support the conclusion that neurotoxins preponderating in the venoms of the *COLUBRIDAE* are more resistant to digestive juices than the other constituents predominating among the venoms of the *VIPERIDAE*.

Influence of temperature on behavior of fish in morphine and cobra venom solutions. David I. Macht (with technical assistance of Ruth Legg). *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* Ichthyometric studies were made on the activity of *Carassius auratus* at different temperatures by methods described elsewhere (J. A. Ph. A., 1941, XXX, 203). Three ranges of temperature were employed: (1) 20 to 25°C., (2) 15 to 20°C. and (3) 25 to 30°C. Experiments with normal controls established the fact that lower temperatures inhibit and warmer temperatures stimulate activity of goldfish. Morphine sulphate was employed in concentrations of 1:5,000 to 1:1,000.. Cobra venom was studied in concentrations by weight of 1:10,000 to 1:300,000 (the potency being 0.01 mgm. per mouse unit). At room temperature, morphine, 1:1,000, was lethal in a few hours while cobra venom was lethal within twelve hours in concentrations below 1:20,000. Fish placed in solutions of morphine, 1:2,000 to 1:5,000, at 20 to 25°C., revealed marked depression and toxicity after an hour's exposure to drug. Colder solutions depressed only after two hours. Warm solutions became depressant in half an hour and markedly depressant in one hour.

Cobra venom solutions, 1:150,000 to 1:300,000, at normal temperatures (20-25°C.), produced little effect. Solutions of 1:80,000 were depressant; concentrations stronger than 1:20,000 were lethal. Solutions of 1:100,000 to 1:300,000 at the lower temperatures (15-20°C.) effected definite stimulation or excitement. At warmer temperatures the same concentrations definitely depressed.

Effect of menotoxin on neuromuscular responses. David I. Macht. *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* Twenty-four rats, twelve male and twelve female, were injected with normal and menstrual blood sera, respectively, care being taken to avoid anaphylactic shock by not using the same animals too often. In three sets of experiments studies were made on 1, the behavior

of rats in a circular maze to discover their activity as well as learning and discriminatory faculty; 2, the effect of drugs on the neuromuscular coordination of the legs of rats walking a tight rope, and 3, the influence of such injections on their ability to climb a perpendicular rope to determine the working capacity of the skeletal muscles. Considerable variation in toxicity was noted in different samples of menstrual blood. All the menotoxic sera, however, markedly affected the behavior of the rats. Doses of 0.25 to 0.50 cc. lengthened the time of performance and increased the number of errors in the maze. In the rope experiments animals injected with menstrual sera exhibited a marked weakness as compared with controls receiving normal serum or normal physiological saline. In the rope-climbing test especially large doses of menstrual blood stalled or completely incapacitated the animals; and two rats, one male and one female, were killed by such injections of menstrual serum.

Sensitization of guinea pigs through male genitalia. DAVID I. MACHT. *Pharmacological Research Laby., Hynson, Westcott & Dunning, Inc., Baltimore, Md.* Twenty guinea pigs were sensitized by subcutaneous injections of horse serum, then allowed to rest from ten to fourteen days, after which the antigen was injected directly into their circulation. With one exception all the animals developed typical anaphylactic shock followed in most cases by death. A series of normal, unsensitized control guinea pigs, similarly injected with horse serum, exhibited no anaphylactic phenomena. A third series of 20 guinea pigs were then treated as follows: Daily applications of 0.2 cc. of horse serum to the preputial sac were made for 10 to 15 minutes for five days, the animals each time being returned to their cages after treatment without washing out the serum. After they had rested from ten to fourteen days, horse serum was injected directly into the circulation of the guinea pigs. All except three animals developed more or less violent anaphylactic shock, thus proving definite sensitization by absorption through the prepuce and penis. Fifteen of the animals died of anaphylactic shock. Complete excision of the prepuce was performed in another series of guinea pigs. After healing of the wounds, horse serum was daily applied to the penis for fifteen minutes on 5 successive days. These guinea pigs exhibited anaphylactic phenomena after a rest period of ten to fourteen days on injection of the antigen but these symptoms while definite were not violent and did not result fatally in most of the cases.

A hitherto unreported spinal reflex of the cat. MARTIN B. MACHT (introduced by Philip Bard). *Dept. of Physiology, School of Medicine, Johns Hopkins Univ., Baltimore, Md.* When a paw of a normal cat is immersed in water it is withdrawn immediately and is usually shaken vigorously. The effective stimulus is tactile, for the response is not influenced by the temperature of the water within the range 0°–45°C. Macht and Bard observed in long-surviving decerebrate cats a paw-withdrawal response which is dependent upon conditions of stimulation distinctly different from those effective in the normal animal. The decerebrate preparation in the chronic state withdraws and shakes its paw only if that paw is immersed in water the temperature of which is at a certain level above or below the body temperature of the animal. In the case of water at a temperature below that of the body, the response is dependent upon a gradient between the temperature of the water and the temperature of the body; the receptors involved are probably Krause's end-bulbs. In the case of water at a temperature above that of the body, the threshold for withdrawal is extremely high, is relatively constant, and is independent of body temperature; the receptors here are probably free nerve-endings.

The non-tactile reflex described above is evocable contralaterally after removal of one frontal pole of the cerebral cortex. It has been observed in long-surviving decorticate, hypothalamic, mesencephalic, pontile, and spinal animals, but none of these preparations ever showed the tactile response. It is concluded that the tactile withdrawal response, seen in the normal animal and dependent upon the functional integrity of the frontal poles, masks a purely spinal reflex.

The effect of sodium cyanide on the formation of the pressor substance of the completely ischemic kidney. C. J. MARIENFELD (by invitation) and G. E. WAKERLIN. *Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.* The release of a pressor substance or substances on reestablishment of the circulation of the completely ischemic kidney has been demonstrated (Taquini and others). There is also evidence for the presence of a pressor substance in perfusates of completely ischemic kidneys (Williams and others). Moreover the formation of pressor amines by the renal cortex under anaerobic conditions has been shown (Holtz and others). The importance of these pressor substances for the pathogenesis of experimental renal hypertension has been suggested.

In view of the possible role of local anoxia in the suggested enzymatic production and release of the pathogenetic pressor substance from the kidneys of experimental renal hypertensive (Goldblatt) animals, we have studied the effect of sodium cyanide on the rate and amount of pressor substance formed in the completely ischemic kidney of cats, both by perfusion and by reestablishment of the renal circulation technics. Sodium cyanide

produced no change in the average threshold time of one-half hour for the consistent demonstration of the pressor substance and no change in its amount when the perfusion technic was used. Similar though equivocal results were obtained with the reestablishment of the renal circulation technic. The results suggest that the enzyme systems inhibited by the concentrations of cyanide used are not involved in the production of the pressor substance of the completely ischemic kidney and constitute negative evidence against a role for anoxia in the release of the pathogenetic renal pressor substance in experimental renal hypertension.

The central inhibitory action of adrenaline and related compounds. AMEDEO S. MARRAZZI (introduced by R. W. Gerard). *Dept. of Physiology, Univ. of Chicago and Dept. of Pharmacology, New York Univ. College of Medicine.* Having found that adrenaline and sympathomimetic amines in general exercise a specific inhibitory action on sympathetic ganglionic synapses, it seemed pertinent to determine whether such an action occurs at synapses of the central nervous system.

The on and off potentials recorded from the optic cortex (Gerard, Marshall and Saul, 1936) on briefly illuminating the contralateral eye in lightly nembutalized cats suffered a marked reduction when adrenaline was injected intravenously. Adrenaline has little effect on cerebral circulation other than to secondarily accelerate blood flow, which would not produce inhibition. Intracranial pressure changes were eliminated.

Localization of the site of action was partly achieved as follows. Potentials evoked by illuminating the eye were recorded directly from the optic tract by concentric electrodes inserted with the aid of the stereotaxic apparatus. These potentials were also reduced by adrenaline, pointing to an action on the eye, probably on the retinal synapses. Next the electrodes in the optic tract were utilized to stimulate the optic pathway exclusive of the eye. Adrenaline again reduced the cortical responses, pointing to an action on one or both of the remaining synapses, the geniculate and cortical. Within the optic pathway, therefore, adrenaline has multiple sites of inhibitory action. Extraocular optic inhibition was also obtained with amphetamine (benzedrine).

Evoked auditory cortical potentials likewise were reduced by adrenaline. Work continues in further localization, in extending the survey of the effects on the afferent flow to the cortex and in determining whether minimal effective doses will place the actions in the physiological and therapeutic ranges. [*Aided by a grant from the Dazian Foundation for Medical Research.*]

The use of cantharides blisters for the study of tissue fluid. H. S. MAYERSON. *Laby. of Physiology, School of Medicine, Tulane Univ., New Orleans, La.* Cantharides plasters were applied to the skin of the forearm or ankle and removed 15 to 22 hours later. The resulting blisters were heavily coated with vinylite resin and cannulated by means of hypodermic needle tubing cemented into the top of a no. 000 gelatine capsule to which small weighed flasks were attached. The blisters were drained and the subsequent rate of fluid formation determined by removing and weighing the flasks at various intervals. The specific gravity was also determined by the falling drop method.

Control observations indicated that the rate of formation and the specific gravity of the fluid were relatively constant for a period of about 4 to 6 hours after the plasters were removed. The rate of formation subsequently diminished but the specific gravity did not change. In many cases, fluid was still being formed in measurable quantities twenty-four to thirty hours later. The rate of flow in the various experiments ranged from 0.006 to 0.14 cc. per sq.cm. per hour and the protein content varied from 2.2 to 5.6 grams per cent. Venous congestion in the arm resulted in an increased formation of fluid which, in several experiments, amounted to over 400 p.c. The total amount of protein present in the fluid also increased significantly. Reestablishment of normal circulation resulted in an almost complete suppression of fluid flow for an hour or more. Direct heating of the arm below the blister with an electric heater increased the amount of fluid formed and its specific gravity. Standing also resulted in a marked increase in the formation of fluid of high specific gravity in blisters placed on the ankles.

These preliminary findings suggest that the procedure offers a convenient and relatively easily controlled method of studying the changes in formation and composition of tissue fluid under many physiological and pathological conditions. [*Aided by a grant from the John and Mary Markle Foundation.*]

Storage of fluorine in human bones and teeth. J. F. MCCLENDON and WM. C. FOSTER (by invitation). *Hahnemann Medical College, Philadelphia.* On an ordinary diet each of us was excreting 1 mgm. fluorine in the urine per day. One of us (J.M.) had 2 molar teeth extracted, the dentin of which contained 0.019 and 0.033 per cent F respectively.

Following this for a period of about 1 year each of us ingested 1 gram of powdered fluorapatite containing 40 mgm. fluorine daily. During this period (J.M.) had 2 more molar teeth extracted, the dentin of which contained 0.042 and 0.047 per cent F respectively.

After 5 weeks (J.M.) excreted 10.3 and (W.F.) 8.4 mgm. F daily and after 10 months (J.M.) excreted 11 mgm. F daily. A week after the last

apatite ingestion (J.M.) excreted 10 mgm. F daily and 2 months later 8 mgm. F daily. Since this is more than could be stored in the teeth it indicates that fluorine was stored in the bones. No toxic effects were observed even when 2.5 times this quantity of fluorapatite was ingested daily for 3 weeks.

Prevention of dental caries by brushing the teeth with fluorapatite. J. F. McCLENDON and WM. C. FOSTER (by invitation). *Hahnemann Medical College, Philadelphia.* Rats on a cracked cereal-milk powder diet containing 0.3 part per million of fluorine developed 3.3 caries per rat in 90 days, whereas rats on the same diet but with their teeth brushed each day with powdered fluorapatite developed 0.3 caries per rat. In 100 days the figures were 3.5 and 0.5 respectively. The dentine of the molar teeth not brushed with fluorapatite contained 0.0069 per cent F whereas that of rats on the same diet but with their teeth brushed with fluorapatite contained 0.08 per cent F, an increase of 11 times. The increase in F in the enamel was about 5 times (0.006–0.033). This indicated that the rats swallowed the fluorapatite, as was also indicated by their more rapid growth and greater health. The enamel of the constantly growing incisors was only slightly higher in fluorine than that of the molars. [*The fluorapatite was given by the Rhum Phosphate and Chemical Co., Mt. Pleasant, Tenn.*]

Fluctuation of cortical oxygen tension during induced convulsions. WARREN S. McCULLOCH and E. ROSEMAN (by invitation). *Illinois Neuropsychiatric Inst.* By recording synchronously the electrical activity of the cerebral cortex, the electrocardiogram and a measure of the current through a negative platinum electrode and a positive Ag-AgCl electrode, due to a voltage selected to fall at the center of the oxygen plateau of the current-voltage curve, the oxygen tension of the cortex was studied during seizures induced with various convulsive agents in animals paralyzed with beta-erythroidine-hydrobromide. Recently concomitant blood pressures have been recorded. The maximum changes in oxygen tension were first obtained by respiration of 5 per cent CO_2 in 95 per cent oxygen and with 100 per cent nitrogen.

Seizures were induced electrically and by intravenous caffeine, aminophylline, coramine, metrazol, picrotoxin and strychnine. In all cases there was a marked fall in oxygen tension, beginning before electrical signs of the seizure, and usually reaching its nadir subsequent to the fit. Thereafter it rose above the pre-seizure level. Only during rapid recurrence of seizures in status did the electrical activity increase before oxygen tension fell. Blood pressure and heart rate studies showed that the fall in oxygen tension could not be attributed to altered systemic circulation. Therefore, it is concluded that the observed fall in oxygen tension is due to the altered metabolism of the cortex, and that the alteration begins before the observed electrical seizure of the cortex.

A further brief note on the presence of leukotaxine in inflammatory exudates. VALY MENKIN. *Dept. of Pathology, Harvard Univ. Medical School, Boston, Mass.* Leukotaxine recovered from exudates induces both increased capillary permeability and prompt migration of polymorphonuclear leukocytes. (Menkin, V. Dynamics of inflammation. Macmillan Co., New York, 1940.) The cutaneous accumulation of a dye, trypan blue, from the circulating blood stream serves as a gauge of the extent of capillary permeability. Recently Freeman and Schecter have shown that a dye, T-1824, present in the blood stream, will accumulate in an area of skin in a dog previously treated with the serum obtained from a different dog. (Freeman, N. E. and A. E. Schecter. Proc. Soc. Exper. Biol. and Med. 51: 29, 1942.) On the other hand, these investigators have pointed out that cutaneous injection of the serum of a given dog followed by introduction of a dye in the circulation of the same animal is not followed by any accumulation of the indicator dye substance. The writer has in his chemical studies been unable to demonstrate the presence of leukotaxine in normal blood serum. (Menkin, V. Dynamics of inflammation. Macmillan Co., New York, 1940.) Nevertheless, in view of Freeman and Schecter's observations, experiments on dogs have been undertaken to determine whether the exudate of a given animal will induce when injected into its own skin an accumulation of trypan blue from the circulation. Similar experiments had already been performed in the past on rabbits (V. Menkin. J. Exper. Med. 64: 485, 1936). The cutaneous introduction in a dog of such an exudate, previously removed from its pleural cavity, is indeed found to be followed by an intense accumulation and local staining of the tissue with dye. Since this reaction fails to occur with its serum, the observation serves as further indication concerning the presence of a substance liberated in exudates which increases capillary permeability (i.e., leukotaxine) and its corresponding absence in the serum of a given animal.

On maternal and paternal inheritance of bodily form in the hybrid plutei of the sea urchins, strongylocentrotus purpuratus and S. Franciscanus. A. R. MOORE. *Dept. Psychology, Univ. of Oregon, Eugene.* In a study published in 1910, Loeb, King and Moore described the bodily form of pluteus of *S. franciscanus* as round-topped with very long ventral arms, while that of *S. purpuratus* was of pyramidal shape with short arms; plutei of the hybrid *purpuratus* ♀ × *franciscanus* ♂ showed rounded top and ventral arms moderately

long. Recently E. B. Harvey has reported her failure to obtain other than maternal inheritance in this cross. Because of the unsatisfactory nature of the evidence submitted by Harvey it seems necessary to re-examine the problem. This was done by making photographic records of the larvae in the five day stage, temperature 13.5° to 15°C. As indicator of bodily form I have used the ratio of body-width to total length, i.e., tip of ventral arm to apex. Measurements were then made on enlarged photographs with a vernier calliper. For *franciscanus* the ratio is 0.603, for *purpuratus* is 0.810, for the hybrid, *purpuratus* ♀ × *franciscanus* ♂, the ratio is 0.646. Therefore, in the hybrid pluteus, the inheritance of bodily form is more nearly paternal than maternal.

Differential effects of stretch upon the stroke volumes of the right and left ventricles. W. GLENN MOSS (by invitation) and VICTOR JOHNSON. *Dept. of Physiology, Univ. of Chicago.* In motion picture studies of the outputs of the right and left ventricles, estimated separately and simultaneously in dogs, this laboratory reported (Am. J. Physiol. 137: 620, 1942) that periodic respiratory fluctuations in output were associated with corresponding fluctuations in diastolic sizes of the right and left ventricles. When the diastolic size of the right ventricle increased, its stroke volume also increased, even though the diastolic size and stroke volume of the left ventricle simultaneously decreased.

Employing the same technique, and varying the diastolic size by several methods, the authors found that the relationship of diastolic size (i.e., initial fiber length) to stroke volume (i.e., fiber shortening) was more direct in the right than in the left ventricle, probably because the peripheral resistance factor in the work done by the heart fluctuates less in the pulmonary than in the systemic circuit. A given increment in diastolic size of the right ventricle was found to be more effective in causing an increased stroke volume than was true of the left ventricle, probably because the muscle fibers of the right ventricle pursue a straighter course than do the fibers of the left ventricle so that a given increase in diastolic size produces a greater actual stretch of the fibers themselves in the right as compared with the left ventricle.

Treatment of experimental renal hypertension with vitamin A preparations. W. G. MOSS (by invitation), E. L. SMITH (by invitation) and G. E. WAKERLIN. *Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.* Striking reductions in blood pressure were observed in three renal hypertensive dogs treated daily with 200,000 units of vitamin A concentrate in sesame oil by mouth for three months, followed by 400,000 units for an additional three months. Two control dogs treated with sesame oil by mouth for six months showed no significant changes in their hypertensive levels. One hypertensive dog showed no significant change in blood pressure after three months of treatment with 400,000 units daily of a highly purified vitamin A preparation by mouth. One hypertensive dog showed no significant change in blood pressure after three months of treatment with heat-inactivated vitamin A concentrate. These preliminary results suggest but do not prove that the antihypertensive activity of the vitamin A concentrate which we have used is due to some heat-labile constituent of the concentrate other than vitamin A.

In view of the therapeutic results with the vitamin A concentrate, a study of its prophylactic effect was also made. Thus far, four dogs have been treated for three months prior to bilateral constriction of the renal arteries with 400,000 units of the concentrate daily by mouth without any effect on the normotensions of the animals. Four control dogs have been treated prophylactically with sesame oil. The results show that the vitamin A concentrate in the dosage used does not protect dogs against the development of experimental renal hypertension produced by constriction of the renal arteries.

No evidences of toxicity from the vitamin A concentrate were detected in any of the animals.

The monkey (Macaca mulatta) after hemisection and subsequent transection of the spinal cord. GRAYSON P. MCCOUCH, JOSEPH HUGHES and WINIFRED B. STEWART. *Dept. of Physiology, Univ. of Pennsylvania and Inst. of the Pennsylvania Hospital, Philadelphia.* A series of 14 macaca mulatta monkeys and one macacus mordax have been studied after hemisection and subsequent transection of the spinal cord. In confirmation of previous work, reflex recovery was always more rapid in the previously paretic extremity. Three animals developed crossed reflexes on the chronic side in response to stimulation on the acute side. Crossed flexion of digits was recorded a few hours after transection; crossed extension of leg two or more days later. Crossed inhibition may be more effectual when driven from the chronic side affecting the acute side than vice versa. Only exceptionally is asymmetry reflected in internuncial potentials; never to the degree obtaining in the corresponding reflex responses. This is consonant with our previous finding that interneurons suffer less severely from spinal shock than do motoneurons. If the last cells to recover be motoneurons, crossed reflexes should find their earliest motor expression upon the side of previous hemisection where recovery is more advanced and in those units which show least depression. Thus digital flexion, which is the first ipsilateral reflex, is likewise the first crossed response. With

crossed inhibition internuncial shock may be a significant factor in recovery. Another may lie in the high susceptibility to inhibition of the motoneuron when its excitability is low. Both influences favor inhibition from a source on the chronic side of previous hemisection acting upon the motor cells of the more depressed side which has suffered almost its entire quota of shock after transection. Results accord with these considerations.

The effect of adrenocortical extracts on the distribution of injected potassium. L. J. MULLINS (by invitation), TERRINE K. ADLER (by invitation) and W. O. FENN. *Dept. of Physiology, School of Medicine and Dentistry, Univ. of Rochester, Rochester, N. Y.* Potassium chloride (1.66 ml of 0.2 M) was injected into the carotid artery of anesthetized rabbits at 20 minute intervals. Just before each injection a sample of blood was taken and the plasma was analyzed for K. The progressive increase in K concentration was thus followed in normal animals and animals pretreated for two days with adrenal cortical extract. (Usually 50 dog units per day and a third similar dose intravenously just before the experiment). The calculated volume of distribution was 99 per cent of the body weight in the normal and 50 per cent in the cortin-treated animals. The difference was not due to excretion of potassium but appeared to indicate a diminished uptake of K by the tissues under the influence of cortin. Thus cortin-treated animals died sooner than the controls because the plasma K concentration was higher. With an intraperitoneal injection of a single large dose of KCl (7.7 mM per kgm.) the cortin had an opposite or protective effect, the injected animals having a slower and smaller increase of K concentration in the plasma. Repetition of these experiments with intraperitoneal injections of radioactive K showed less radioactivity in the muscles of the cortin-treated animals. Superficially considered these experiments appear to show that cortin decreases the transfer of K from peritoneum to plasma or from plasma to tissues. Tentative experiments indicate that desoxycorticosterone has an effect similar to cortin when administered in olive oil but is without effect when given in alcohol.

The failure of asparagine to protect guinea pigs from the lethal effects of anoxia. DOROTHY NELSON (introduced by A. C. Ivy). *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* We have found that a carrot diet prolongs the survival of guinea pigs exposed to acute anoxia. Campbell obtained evidence indicating that the cellulose content of carrots is partially responsible for their beneficial effects in the case of rats. It seemed possible that succinic acid, one of the principle residues from the break down of cellulose might account for the carrot's protection against anoxia because of its important role in the oxidation-reduction processes. To test this hypothesis the following investigation was undertaken.

Two groups of 7 male guinea pigs (A and B) were given a diet of Purina rabbit chow and milk (ad libitum). This diet was previously found to be detrimental compared to a carrot diet. Group A was fed daily by tuberculin syringe 1500 mgm. l-asparagine in syrup. Group B received syrup only. Asparagine is used interchangeably with succinic acid in cellular metabolism and is better tolerated by the animals. The dose was based on the maximal amount of succinic acid obtainable from the estimated quantity of carrots eaten in the previous experiment. A control group, C, (10 males) was given Purina rabbit chow, carrots and greens.

After 3 weeks on these regimes the animals were exposed (decompression chamber) for 1 hour to each of the following pressures: 178.7, 170.4, 162.4, 154.9, and 147.6 mm. Hg. The survival was as follows: Group A, 19 per cent; B, 14 per cent; C, 90 per cent. *Conclusion:* Asparagine fed to guinea pigs does not protect them against the lethal effects of anoxia. [*Assisted in part by a grant from the Abbott Fund of Northwestern University.*]

Maintenance of corpora lutea in hypophysectomized rats by lactogenic hormone. WARREN O. NELSON and J. WALTON PICHETTE (by invitation). *Wayne Univ., College of Medicine, Detroit.* It is possible to induce a condition of pseudopregnancy in adult female rats by the administration of estrogenic hormone. The phenomenon appears to be due to the release of luteotrophin from the hypophysis and not to any direct effect of estrin on the corpus luteum (Nelson and Pichette, 1942). Animals in which pseudopregnancy has been induced by the continued administration of estrin return to estrus within a few days after hypophysectomy. As a further test of the primary importance of the hypophysis in the reaction luteotrophin (lactogenic hormone) was used to substitute for the hypophysis in hypophysectomized animals.

Twenty-four animals received 200 I.U. estrone (Theelin) daily, treatment in each instance being instituted during estrus. Eight animals received no further treatment. They maintained periods of pseudopregnancy for 14 to 19 days before assuming continuous estrus. Sixteen animals were hypophysectomized on the 7th to 9th day after the initiation of treatment. Five animals which received only estrone returned to estrus on the 3rd or 4th day after operation. The remaining eleven animals received 10 mgm. lactogen daily for 7 to 17 days, starting with the day of hypophysectomy, in addition to estrone. Without exception luteal function, as shown by examination of the mammary glands, vagina, uterus and ovaries, was maintained throughout the period of treatment. In

four instances lactogen was withdrawn, estrone being continued. Estrus occurred three days later.

These results affirm the importance of the hypophysis in the maintenance of corporalutea in animals treated with estrogenic hormone.

The effect of anoxia on the activity of the colon. DAVID W. NORTHUP, EDWARD J. VAN LIERE and J. CLIFFORD STICKNEY (by invitation). *Dept. of Physiology, School of Medicine, West Virginia Univ., Morgantown.* The action of acute anoxia on the activity of the colon of the dog has been studied. Movements of the longitudinal muscles were recorded by a device described by Lawson. Anoxia was produced by having the animals breathe oxygen-nitrogen mixtures made in an anesthesia machine. In a few experiments a rebreathing apparatus with soda lime absorber was used. Concentrations of oxygen ranged from about 6 to 15 per cent.

Concentrations of 13 to 15 per cent O_2 had little if any effect other than slight loss of tone. This evidently represents the threshold for the effects. It corresponds to an altitude of from 9,000 to 12,000 feet. Lower concentrations depressed the rhythmic activity; at the lowest oxygen tensions used contractions were practically abolished. Occasionally a brief initial stimulation was seen. When the animals were again allowed to breathe room air, about half of them exhibited a strong spasm of the longitudinal intestinal muscles, lasting approximately 15 minutes.

Chronic hypoxia in the cat. ROBERT H. OSTER and J. E. P. TOMAN (by invitation). *Dept. of Physiology, Univ. of Maryland School of Medicine, Baltimore.* Mature healthy cats showed marked resistance to hypoxia. Survival times (to respiratory failure) varied from 14 to 60 minutes at 3.5 ± 0.1 per cent oxygen, among different animals, with a mean value of 31 minutes. Some animals showed acclimatization of as high as 80 per cent after 6 or more daily tests. 4.6 per cent oxygen was found to be the lowest concentration at which consciousness could be maintained for two hours. (At the same rate of gas flow pure nitrogen produced respiratory failure in 2 to 4 min.)

Of 50 animals subjected to 157 hypoxia tests, only 6 failed to recover with artificial respiration. Five animals, after 12 to 21 daily exposures, showed lasting impairment (blindness, deafness, cachexia, anorexia, and general reflex depression). Two such animals, maintained for several months, improved considerably, but developed permanent hyperactivity and a stereotyped cage-scratching behavior pattern. Electrocorticograms showed continuous 3-per-second dysrhythmia compared with normal cats at the same anaesthetic stage. Brain sections revealed a small but significant percentage of chromatolysis in all neocortical layers, particularly in the outer pyramids and granules, and most marked in the primary visual area. Damage was also marked in lateral geniculate, and moderate in superior and inferior colliculi, thalamic midline nuclei, medullary reticular formation, and nucleus gracilis. [*Supported by a grant from the Bressler Alumni Research Fund.*]

Electroencephalographic observations associated with large intravenous injections of acetylcholine in mental patients. BERNARD L. PACELLA and MEYER M. HARRIS (introduced by S. E. Barrera). *Dept. of Psychiatry and Internal Medicine, New York State Psychiatric Inst. and Hospital.* Studies were carried out on 8 patients who received intravenous injections of acetylcholine in doses ranging from 80 to 490 mgm. A total of 13 electroencephalographic studies were made on this group associated with injections of acetylcholine. In addition to this EEG recordings were made before, after, and in two instances during the course of acetylcholine therapy. (Courses varied from 19 to 61 injections given daily 5 times a week, week-ends being omitted.) The observations, therefore, may be divided into two groups. First, those associated with the individual injection of acetylcholine and second, those resulting from a course of treatment.

It was found that only those cases which received relatively large doses of acetylcholine (over 120 mgm.) sufficient to produce cardiac arrest for periods ranging from 6 to 40 seconds resulted in very temporary alterations of the EEG pattern consisting of slow, high amplitude potentials. These potentials usually appeared after 6 to 15 seconds of cardiac arrest and persisted about 10 to 20 seconds after regular cardiac rhythm was established. Subsequent to this most EEG records exhibited an increase in the alpha amplitude and incidence for varying periods up to $\frac{3}{4}$ of an hour of observation. In those cases which did not show any cardiac arrest following acetylcholine injection little or no changes in the electroencephalogram resulted. This latter observation is similar to that reported by other investigators for normal individuals and is in contrast to the observations reported for epileptic patients.

After a complete course of acetylcholine injections there did not seem to be any appreciable alteration in the electroencephalographic pattern from that which was observed prior to treatment.

The occurrence of a vasoconstrictor substance in blood during shock induced by trauma, hemorrhage and burns. IRVINE H. PAGE. *Lilly Laby. for Clinical Research, Indianapolis City Hospital, Indianapolis, Ind.* Shock, whether elicited by tourniquets placed around the extremities, stripping and exposing the intestines, hemorrhage and burns, is associated with the appearance in the plasma of a substance which causes

vasoconstriction in rabbits' ears perfused with either calcium-free Ringer's solution or plasma. It does not originate in the kidneys, adrenal glands, nor does destruction of the spinal cord or renal denervation prevent its appearance. Evidence gathered from application of a method depending on fatiguing the vascular musculature suggests, if the validity of the method is acceptable, that the vasoconstrictor action of plasma from burned, bled and shocked dogs is caused by identical or very similar substances. Furthermore, it differs from the vasoconstrictors present in hypertensive's (human and canine) plasma and in serum (human and canine). None of these vasoconstrictors seem to be histamine.

The diuretic action of thyroid in diabetes insipidus. DONALD PHILLIPS (by invitation) and KENDRICK HARE. *Dept. of Anatomy, State Univ. of Iowa, Iowa City.* Dried thyroid has been added to the diet of three groups of dogs (1) normal, (2) latent polyuric, and (3) with severe diabetes insipidus. Complete destruction of the pars nervosa produces dogs with severe diabetes; partial destruction results in a dog relatively deficient in antidiuretic hormone. Under ordinary circumstances this animal has a normal or slightly increased water exchange but, under the stress of thyroid or saline administration, develops a severe polyuria.

Thyroid feeding increased the creatinine clearances of all three groups by about the same amount. In group 1 the urine flow was only slightly increased; in group 3 it was increased by about the same percentage as glomerular filtration. In group 2 the urine flow was increased as much as 40 fold when glomerular filtration was only doubled. Therefore a part of the diuresis is due to a diminished tubular reabsorption of water. The chloride R/P in groups 1 and 3 is not altered, but in group 2 it is progressively elevated over a period of 2–3 weeks toward that of a dog with diabetes insipidus. Two possibilities are evident; the thyroid decreases the formation or liberation of the pituitary antidiuretic hormone or it interferes with the action of pituitrin on the renal tubules. Only the latter has been studied. Dogs with severe diabetes insipidus concentrate their urine, as measured by creatinine U/P, on the injection of as little as 0.1 milliunit of Pitressin. The same dogs failed to respond to 20 milliunits when they were fed thyroid.

The influence of liver damage, by chloroform, on pentothal sodium in guinea pigs. GRADY W. PHILLIPS (by invitation), MARK C. WHEELOCK (by invitation), and EMMETT B. CARMICHAEL. *Depts. of Physiological Chemistry and of Pathology, School of Medicine, Univ. of Alabama, University.* A 26.66 per cent solution of chloroform in olive oil, in varying doses from 0.3 cc./kgm. to 0.5 cc./kgm., was injected intraperitoneally into 24 normal well fed adult guinea pigs at intervals of 3 to 4 days until 2 to 4 doses had been injected. Food was provided at all times to prevent inanition. Pentothal in doses of either 45 mgm./kgm. or 50 mgm./kgm. was injected intraperitoneally 3 to 4 days after the last injection of chloroform. The animals were kept warm and those that died were autopsied at once and those that survived the barbiturate were allowed to eat and then were terminated. Histologic studies gave evidence of liver damage for all animals that received chloroform. The kidneys of these animals showed no damage. Five of the 24 animals died after receiving the pentothal which is about the same per cent of deaths for normal animals that receive these same doses of this drug.

The duration of hypnosis in control animals was 7 to 8.5 hours with an average of about 8 hours, for the above doses, whereas the chloroform injected animals, with the exception of one whose hypnosis lasted 7.5 hours, had a hypnosis lasting from 9.5 to 21 hours. The average length of hypnosis of the animals that lived under both doses of pentothal was about 12 hours. This shows an increase in the duration of hypnosis of about 50 per cent above the normal duration of hypnosis for these doses of pentothal.

The effect of ischemia on neuro-muscular response. E. L. PORTER and E. L. CALLAHAN (by invitation). *Dept. of Physiology, Medical School, Univ. of Texas, Galveston.* In some recent studies on arterial pain, we appeared to be demonstrating that ischemia caused an increased reflex response as evidenced by a higher contraction of the tibialis anticus muscle which was being used as an indicator. Upon testing this muscle as a nerve-muscle preparation, however, we found that ischemia caused an increased height of contraction here also. The curarized muscle did not show this effect under ischemia. Neither was it an effect on the nerve, since the circulation in the nerve could be seen to continue during the muscle ischemia. We have concluded, therefore, that ischemia causes an improved conduction through neuro-muscular junctions. This action would be similar to that caused by asphyxia on the synapses of the cord. It suggests that the pain accompanying intermittent claudication may be due in part to an action on neuro-muscular junctions, with a resultant over-contraction of the muscle.

The effects of hyperventilation and of blood pressure changes on self-sustained responses of the cerebral cortex. E. C. DEL POZO and A. LEÃO (introduced by H. Davis). *Dept of Physiology, Harvard Medical School, Boston, Mass.* These effects were studied in cats under dial anesthesia. Multiple electrical records were taken from 2 to 6 pairs of electrodes placed on the pia of

one or both hemispheres, with capacity-coupled amplifiers and ink-writing galvanometers. The stimuli were trains of induced shocks delivered to the cortex.

Hyperventilation produces a marked decrease of the self-sustained responses (Rosenblueth and Cannon. Am. J. Physiol. 135: 690, 1942). The decrease occurs simultaneously in all the active regions. The duration of the response is shorter; the voltage and frequency of the potential changes are reduced. The spontaneous activity is also reduced by hyperventilation. These changes are reversible. One to three minutes of hyperventilation are usually sufficient to produce the effect.

Hyperventilation causes a fall of blood pressure. Falls of blood pressure produced by vagal stimulation or compression of the heart are attended by a decrease of the cortical responses. However, when the fall of blood pressure caused by hyperventilation is prevented by compression of the aorta, a decrease of the self-sustained activity still occurs.

Overbreathing without acapnia (gas mixtures with 4 to 8 per cent CO_2) does not lower the blood pressure, and fails to reduce the cortical responses.

It is concluded that acapnia diminishes the self-sustained responses and the spontaneous activity of the cortex.

The response of the pyloric sphincter region to emotions and noxious bodily stimuli. J. P. QUIGLEY and (by invitation) H. J. BAVOR, M. R. READ and B. L. BROFMAN. *Dept. of Physiology, Western Reserve Univ. Medical School, Cleveland, O.* Reports by previous investigators indicate that pylorospasm is readily produced by noxious stimuli applied to almost any portion of the body. These reports, however, were based on indirect observations or on experiments performed on anesthetized animals.

In a series of dogs trained to participate in the experiments, we have reinvestigated this problem with tandem balloons inserted in the pyloric region and also by the roentgenological observation of the shadow of lead shot stitched to the serosa at either side of the sphincter (pyloric diagraph method). The process of gastric evacuation was also observed and the antral and bulbar pressures measured. The effect of emotional upsets, of agreeable or disagreeable stimuli applied externally or the distention of several parts of the digestive tract was studied in both fed and fasting animals.

In the unanesthetized, normal animal, the invariable result was an inhibition of the motility and tone of the entire pyloric sphincter region (antrum, sphincter and bulb). Gastric emptying was also suspended during this period of pyloric region inhibition. The duration and magnitude of the response tended to parallel the strength of the stimulus. Contrary to previous reports, in this investigation, pylorospasm was not easily produced. The delay in the evacuation of stomach contents induced by emotions or noxious bodily stimuli resulted from a cessation of gastric peristalsis. It did not involve a spasm of the pyloric sphincter; in fact, it occurred in spite of sphincter relaxation. [*This investigation was aided by a research grant from the Council on Pharmacy and Chemistry.*]

Thyroid feeding and NaCl balance in experimental diabetes insipidus. C. E. RADCLIFFE (introduced by W. R. Ingram). *Dept of Anatomy, State Univ. of Iowa, Iowa City.* Daily NaCl balances were followed over considerable periods in normal cats and cats with diabetes insipidus under standard conditions and during thyroid feeding. Thyroid feeding in DI cats increased the polyuria considerably. At the onset of thyroid feeding there was a transient period of increased NaCl output, but as the urine volume was elevated the NaCl output fell so that for the duration of the enhanced polyuria the NaCl balance was positive and there was an actual retention of NaCl. The same was true in normal cats, but with no diuretic response.

DI cats after thyroidectomy had average urine volumes which were 25–35% less than the previous polyurias but still 3 to 4 times the output of normal cats. The NaCl excretion was slightly altered, the curve approaching a mirror image of that obtained during and after thyroid feeding.

Associated with thyroid feeding there was a rise in the excretion of nitrogen in both normal and DI cats. This increased nitrogen output, however, does not fully parallel the curve of diuresis, cannot fully account for the increased urine volume, and is probably no more than a contributory factor in the increased glomerular filtration rate which follows thyroid feeding.

Similarities in the effects of thyroid feeding and of the ingestion of large quantities of salt in the DI animal were noted.

Electrocardiographic changes during sustained anoxia. WALTER C. RANDALL (introduced by Carl J. Wiggers). *Dept. of Physiology, Western Reserve Univ., Cleveland, O.* Electrocardiographic changes during *sustained anoxia* were studied in barbitalized dogs. Progressive reduction of the oxygen per cent in a respirometer to any desired level was accomplished by rebreathing, CO_2 being absorbed. Animals were maintained at such chosen levels by continuously admitting oxygen into the respirometer in amount equivalent to that being used. Individual resistance varied; some dogs collapsed after short exposures to 12 to 13 per cent oxygen, while others withstood long exposures at 6 to 8 per cent. Length of exposures were varied from 20 minutes to 7½ hours, after which time the dogs were returned to air.

The first prominent electrocardiographic change

was a definitely decreased voltage in the R-wave, often becoming lower than the P and T-waves. With continued anoxia, slurring or splintering appeared, sometimes during rebreathing but more often later in sustained anoxia. Splintering was occasionally noted in the normal record, but with anoxia the splint shifted counter-clockwise and became more severe. Such changes in R-wave have not previously been described. Depression of the T-wave and ST-segment, or a diphasic T, sometimes occurred during rebreathing. More prominently, however, the ST-segment shortened and inclined upward, becoming incorporated in the T-wave as T-voltage was enormously increased during severe anoxia. The P-R interval shortened slightly with accelerated heart rates, lengthening only as terminal heart block became imminent. The electrocardiogram sometimes returned to normal after short exposures but failed to do so after long exposures.

Relation between gastric potential and gastric secretion after histamine. W. S. REHM (introduced by Hampden Lawson). *Dept. of Physiology, Univ. of Louisville School of Medicine, Louisville, Ky.* A lucite chamber was made in two parts which could be fastened together across the wall of the stomach permitting an intact blood supply to that portion in the chamber. Normal saline was placed in the chamber and 100 ml. portions of saline were run through the chamber at 10 minute intervals. H^+ secretion was determined by measuring the pH, free and total acidity of the 100 ml. portions of saline. A non-polarizable electrode was connected to the chamber and another similar electrode was placed against the serosa. Potentials were measured with a potentiometer. Under these conditions there was no evidence of a resting secretion of H^+. Injection of histamine was followed in all cases by a decrease in the magnitude of the potential and a lowering of the pH of the saline. After the response to a single injection the potential and secretion gradually returned to their original levels. With repeated injections the potential and secretion could be maintained at their new levels for the duration of an experiment. The decrease in the potential ranged from 31 per cent to 47 per cent. The average potential before histamine was 71 mv. and after histamine was 43 mv. The average pH of the 100 ml. portions of saline was 3.0 after a relatively constant rate of secretion had been reached.

Effect of thiocyanate on gastric potential and secretion. W. S. REHM and A. J. ENELOW (introduced by Hampden Lawson). *Dept. of Physiology, Univ. of Louisville School of Medicine, Louisville, Ky.* In another communication (Federation Proc. 2: p. 40, 1943) evidence has been presented for a relation between gastric potential and gastric secretion after histamine stimulation. It has previously been shown by several groups of workers that thiocyanate inhibits gastric secretion. A further testing of the hypothesis that there is a relation between gastric secretion and gastric potential was undertaken by studying the effect of thiocyanate on potential and secretion. The same technique for measuring secretion and potential was used as described in the other communication (loc. cit.). Regularly repeated injections of histamine were given and after the rate of secretion had reached a relatively constant level, thiocyanate (0.22 gm. per kgm.) was injeced intravenously. This was followed by a decrease to 0 of the secretion rate, and a concommitant return of the potential, after an initial relatively small decrease to its original pre-histamine level. In order to determine whether the effect of thiocyanate was independent of the secretory activity of the stomach its effect on the resting potential was investigated. A small dose of histamine was injected to make sure that the stomach was capable of secreting and after the stomach had returned to the non-secreting condition, thiocyanate was injected. No effect on the potential was observed. Subsequent injections of histamine after thiocyanate were without effect on the potential and did not produce secretion.

The rôle of liver and kidney in the action of dicumarol (3,3′-Methylene-Bis-(4-hydroxycoumarin)). RICHARD K. RICHARDS and F. R. STEGGERDA. *Abbott Laboratories, North Chicago, Ill.* The action of Dicumarol (3,3′-Methylene-Bis-(4-Hydroxycoumarin)) has been studied in different species of animals and in humans. Its depressing effect upon the blood prothrombin level has so far been found to be the only outstanding property of this compound. The mechanism of action and the fate of the drug in the organism are not yet known. The role of kidney and liver was studied in a large number of rats.

A progressive, subacute liver damage was produced by daily injections of CCl_4; this is accompanied by a slight depression of plasma prothrombin after a number of injections. A standard dose of Dicumarol (2.5 mg.) was given to such rats and their prothrombin time determined 24 hours later, an increasingly greater response to Dicumarol occurred indicating the possibility of an excessive depression of the prothrombin level at a degree of liver damage which shows by itself no or an only slightly elevated prothrombin time.

Unilateral nephrectomy was without influence upon degree or duration of action of Dicumarol; following bilateral nephrectomy, the response after 24 hours was the same as in normal rats. However, from then on the prothrombin content continued to fall in nephrectomized animals until their death, while in unoperated rats the prothrombin level had reached its lowest point after 24 hours and returned

to normal within 48 hours after administration of the drug.

Extraventricular control of the ventricular electrocardiogram. I. Application of KCl to the auricles. JANE SANDS ROBB and ROBERT C. ROBB (by invitation). *Dept. of Pharmacology and Hendricks Research Fund, College of Medicine, Syracuse Univ., Syracuse, N. Y.* Granted that S-T shifts in the electrocardiogram may be obtained by application of KCl to the ventricle, it was not hitherto known that identical effects may be obtained by similar application to the auricles. Furthermore, in the latter instance, we have observed either elevation or depression of S-T both before and during complete heart block. The P wave amplitude may either increase or decrease, auricular S-T may be slightly elevated or depressed, and the auricular T may be more positive or more negative. Local anesthetics of the cocaine series applied to the auricles produce the same changes as KCl, i.e., a "coronary" type of record. Because the ventricular complex may be modified by disturbances in the auricles even when the Bundle of His is experimentally sectioned, we conclude that there must be pathways to the ventricle which do not accompany the Bundle of His.

Extraventricular control of the ventricular electrocardiogram. II. The effect of nicotine applied to the auricles. ROBERT C. ROBB (by invitation) and JANE SANDS ROBB. *Dept. of Pharmacology and Hendricks Research Fund, College of Medicine, Syracuse Univ., Syracuse, N. Y.* All autonomic ganglia are first stimulated and then paralyzed by nicotine. Its application to various areas of the mammalian auricles can initiate an ectopic auricular rhythm often with aberrant conduction to the ventricle, and also ST and T wave changes. The rate is immediately accelerated and later slowed. Because all these effects can occur after section of the vagi and atropine have inactivated the parasympathetic system, the sympathetic system seems implicated. Nonidez (Am. J. Anat. 65: 361, 1939) has described the sympathetic innervation of the heart. In a personal communication he states that there are pale staining cells in the auricles, which may be sympathetic ganglion cells similar to the small ganglia known to have wandered from the larger ganglia to occupy a more peripheral position along the cardio-sympathetic nerves. These subendocardial sympathetic trunks are distributed to the ventricular muscle as well as being coronary vasodilators. In atropinized dogs each successive application of nicotine first increases and then decreases the heart rate. As larger areas of the auricles become paralyzed the ST patterns also vary and the heart rate may eventually become slowed to 10 or 12 per minute. It seems probable that the changes of ST as well as the slowed rate may be due to suppression, of activity in these sympathetic nerve cells. This study seems to indicate the presence of sympathetic ganglia in the auricles with postganglionic ventricular terminations.

Extraventricular control of the ventricular electrocardiogram III. Application of KCl to the cardiac plexuses. JANE SANDS ROBB and M. S. DOOLEY (by invitation). *Dept. of Pharmacology and Hendricks Research Fund, College of Medicine, Syracuse Univ., Syracuse, N. Y.* To establish the implication that KCl, or local anesthetics or nicotine when applied to the auricle cause ST and T changes by action on the sympathetic supply to the ventricle, M/5 KCl was applied to the cardiac plexuses along the great vessels. In atropinized dogs with the vagi cut, and the pericardium intact, M/5 KCl applied to the plexuses alters the form of the ventricular electrocardiogram producing either elevation or depression of ST and either a more positive or more negative T, depending on the region treated. In some experiments, 6 galvanometers were used simultaneously, three to record action currents and three with tight strings (10 mv. = 1 cm.) to record direct current; the control boxes were untouched during the experiments so that shift of base lines gives a measure of injury currents. When KCl is applied to the ventricle, injury currents up to 30 m.v. are often recorded in the standard indirect leads. When KCl is applied to the nerve plexuses and thus ST levels become changed, there is no readable amount of injury current recorded in any one of the 3 standard leads. The ST shifts have been as great as 2 mv., the average 0.5 or 0.6 mv. One must conclude that when the sympathetic cardiac plexuses are treated with M/5 KCl (or cocaine) not only does the heart rate become less but there is also an effect on ventricular muscle which is reflected in the ventricular waves of the electrocardiogram.

Extraventricular control of the ventricular electrocardiogram. IV. The effect of stimulation or excision of the stellate ganglion (and accelerator nerves). J. S. ROBB and A. H. HEGNAUER. *Depts. of Pharmacology and Physiology, Hendricks Research Fund, College of Medicine, Syracuse Univ., Syracuse, N. Y.* Rothberger and Winterberg, Otto, Jannesco and Ionescu, and more recently, Puddu and Chamberlain, have reported on these procedures. Without exception stimulation of the sympathetic is reported to change the electrocardiogram. Most authors find right-sided stimulation more effective; left-sided, more variable; while that of the two sides is generally opposite. Excision of the ganglia is usually reported not to alter the electrocardiogram, but Danielopolu and Marcu oppose this view.

In our experiments on vagotomized, atropinized dogs, excision had less effect than was obtained by nicotine. At first, nicotine stimulated the ganglia

inducing rapid auricular rates, premature auricular beats, or sometimes an ectopic auricular rhythm with aberrant ventricular conduction. Later the rate slowed and S-T displacements occurred. We confirm Rothberger and also Otto in observing more than one ECG pattern resulting from stimulation of one side.

We conclude that the sympathetic nerves do more than merely regulate the heart's force and rate. It seems obvious that these serve as the mechanism integrating the right and left heart chambers, and determine, to a considerable extent, the form of the electrocardiogram.

Potential changes in the olfactory brain produced by electrical stimulation of the olfactory bulb. JERZY E. ROSE (by invitation) and CLINTON N. WOOLSEY. *Neurological Laby. of the Phipps Psychiatric Clinic and Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* A lateroventral dissection of the cat's head was made to bring into view the basal olfactory structures. Other dissections exposed the medial aspect of the hemisphere and Ammon's formation.

On electrical stimulation of the olfactory bulb responses were recorded from the surfaces of the olfactory tract, the prepyriform, the periamygdalar and the entorhinal areas of the hippocampal gyrus. No responses were observed in the retrosplenial area, the olfactory tubercle, the diagonal band or in Ammon's formation.

In the olfactory tract and prepyriform area the responses were surface negative and spikelike, sometimes with two distinguishable peaks. This double spiked response was the characteristic wave form in the medial part of the hippocampal gyrus. Here the peaks were clearly separated, with the second larger than the first. Laterally, in the lateral periamygdalar area, the first spike practically disappeared while the second remained prominent. In addition, in this portion of the hippocampal gyrus a slow surface positive wave followed the spike. The responses in the entorhinal area were small and resembled those of the medial part of the hippocampal gyrus.

Skin temperatures of the extremities in induced deficiencies of thiamine, riboflavin and other components of the vitamin B complex. GRACE M. ROTH, R. D. WILLIAMS and CHARLES SHEARD. *Mayo Foundation and Clinic Rochester, Minn.* Disturbances of vasomotor responses of the feet have been reported by Wenckebach, Weiss and Wilkins, and Wilkins and Kolb on patients suffering from peripheral neuritis associated with vitamin deficiency.

As a part of cooperative study on induced isolated vitamin deficiency states, vasomotor disturbances of the extremities as measured by skin temperatures were carried out on eight physically healthy women for a period from 205 to 253 days in the nutrition division. For the purposes of this study, the subjects were divided into four groups of two subjects each. In group 1 observations were made on the effect of severe isolated restriction ot thiamine; in group 2, on the effect of deficiency of thiamine on induced hypermetabolism; in group 3, on the effect of isolated restriction of riboflavin; and in group 4, on the effect of restriction of vitamin B complex. The criteria for determining the degree of vitamin deficiency were those used by Williams et al., namely (1) the depletion of tissue stores of the vitamin (2) the biochemical defect as a result of the vitamin deficiency (3) the development of polyneuritis.

Under controlled environmental, postural and metabolic conditions, none of the subjects in any group showed any degree of vasomotor disturbance as evidenced by measurements of skin temperature and determinations of rates of cooling and warming. Furthermore, skin temperatures of the extremities of these individuals measured at the height of the state of deficiency and following the administration of vitamin showed a closer correlation with the basal metabolic rate than with the state of vitamin deficiency.

Potassium in metabolism of baker's yeast. ASER ROTHSTEIN and LORRAINE HAEGE (introduced by W. O. Fenn). *Dept. of Biology, and the Dept. of Physiology of the School of Medicine and Dentistry, Univ. of Rochester, Rochester, N. Y.* Aerated yeast in buffered medium (0.02 M K citrate, pH 5.0) plus dextrose gains 6–7 m.eq. per cent (milli-equivalents per 100 cc. of cells) of K^+ from the medium within 10 minutes, and loses 6–7 m.eq. per cent H^+. In 0.03 M KCl (unbuffered) 2–3 m.eq. per cent K^+ and H^+ are exchanged, and the pH drops to 2.7–2.8.

The "initial exchange" of K^+ and H^+ is the same, when available dextrose ranges from 9–80 m.eq. per cent, under anaerobic conditions, and with alcohol as substrate. When less than 35–40 m.eq. per cent sugar is available, a reverse exchange (K^+ out; H^+ in) follows the "initial exchange." When more than 40 m.eq. per cent sugar is available the exchange of K^+ and H^+ continues at a lower rate, but in the same direction as initially, until all the sugar has disappeared. With 60 m.eq. per cent available sugar (maximum used) 16 m.eq. per cent K^+ is accumulated by the cells. One quarter of the available sugar is converted to reserve CHO and the mols of K^+ retained by the cells equals mols of dextrose converted to reserve CHO.

Anaerobic yeast forms half as much reserve CHO and only half as much K^+ is retained. Five-ten-thousandths M NaN_3 or 0.001 M 2:4 dinitrophenol prevent formation of reserve CHO and also prevent exchange of K^+ and H^+. Starving yeast de-

pletes reserve CHO and one mol of K^+ is lost and one mol of H^+ gained for every mol of CHO used (in terms of dextrose).

Measured changes in distribution of phosphate within the cell, which accompany metabolism, can account for only a small fraction of changes in K^+. The "initial exchange" is probably associated within production of an acid during the breakdown of sugar.

The relation of area 13 of the orbital surface of the frontal lobes to hyperactivity and hyperphagia in monkeys. T. C. RUCH and H. A. SHENKIN. (Charles H. Frazier Travelling Fellow 1941–42.) (by invitation). *Laby. of Physiology, Yale Univ. School of Medicine, New Haven, Conn.* The posterior half of the orbital gyrus has recently been differentiated physiologically and cytoarchitecturally, and has been designated area 13 by A. E. Walker. This or adjacent regions were ablated in a series of 5 monkeys after ligation of the sagittal sinus at its anterior end and section of the falx cerebri. Initially, random cage activity is sharply reduced in variety and quantity as is emotional behavior, and the monkeys appear unaware of the environment or human presence. From the first postoperative day this stage is periodically interrupted by bouts of slow, methodical pacing which steadily increase in rate and duration until such pacing is virtually incessant. Such hyperactivity was objectively recorded. It persists for months. Control experiments were 1, ligation of the sinus, 2, blation of the tip of the frontal pole and 3, ligation of the sinus and ablation of the neighboring gyrus rectus. Area 13 lesions were without effect on food intake, O_2 consumption and the rate of carmine passage through the G–I tract. The immediate onset, the intensity and the persistence of hyperactivity indicates that area 13 is of especial importance in the production of hyperactivity. [*Aided by a grant from the Fluid Research Fund, Yale University School of Medicine.*]

The effect of temperature on muscular latency-relaxation. ALEXANDER SANDOW and A. G. KARCZMAR (introduced by Harry A. Charipper). *Washington Square College of Arts and Science.* The following aspects of the latency-relaxation of the frog sartorius have been measured over the range, 10°–40°C.: L_R, the time from stimulation to the beginning of the relaxation; L_T, a similar interval to the first sign of tension development; and R, the magnitude of the relaxation. The L's vary inversely with temperature. Typical values at the extremes of the range are: L_R, 2.5 and 1.2 ms.; L_T, 3.9 and 1.5 ms. R first increases with temperature up to about 22–24°C.; it then falls at higher temperatures until at 40° it is but a few per cent of the maximum value. The maximum of R occurs at about the same temperature as that at which there normally occurs a minimum of the isometric tension. If a muscle that has been kept at 40° for several minutes is then returned to a lower temperature (25°), the values of the L's tend to take on the values characteristic of the lower temperature, but the value of R is only partially restored.

These results indicate the presence of three processes during the latent period: (1), an initial process without mechanical effect that leads into (2), a process that causes the relaxation, and (3), the tension producing process. The temperature variation of R suggests that the relaxation process is subject to a reversible temperature inactivation, and this indicates that an enzyme, probably adenosinetriphosphatase, is connected with the process. [*Aided in part by a grant from the Penrose Fund of the American Philosophical Society.*]

Latency-relaxation in veratrinized muscle. ALEXANDER SANDOW and A. G. KARCZMAR (introduced by Harry A. Charipper). *Washington Square College of Arts and Science.* The latency responses have been studied in frog sartorii at 22°C. when subjected to an activity routine that includes first a series of maximal twitches at one minute intervals, then at ten minute intervals, and finally a series of one second twitch-pairs at ten minute intervals. Each of the twitch pairs consists of two successive maximal twitches separated by a one second interval. Each muscle is studied after first soaking in normal Ringer's solution, and then after 1 hours soaking in a Ringer-veratrine solution, whose veratrine concentration has been varied from 5×10^{-4} to 5×10^{-7}.

The latency behavior of the first twitch of a veratrinized muscle is normal both in its time relations and the magnitude of its relaxation (R), even though the isometric tension output shows the usual veratrine potentiation, double peak, and prolonged post-contractile relaxation. Veratrine affects the latency behavior only if the muscle has been just previously activated, and then, in general, the effect is only to reduce R; the time relations for the beginning of relaxation and for the tension development during the latent period are unchanged. The veratrine effect on R is most pronounced, the closer is the test twitch to the conditioning activity. In general the effect of veratrine seems to be directly proportional to the log of its concentration. These results indicate that in some respects the effects of veratrine on latency-relaxation and on post-contractile-relaxation are similar. Further tests are in progress to critically test this, at present, tentative conclusion. [*Aided in part by a grant from the Penrose Fund of the American Philosophical Society.*]

Studies on the mechanism of cobalt polycythemia. QUINTON D. SCHUBMEHL (by invitation), I. ROBERT WOOD (by invitation) and CHARLES

O. WARREN. *Depts. of Anatomy and Physiology, Cornell Univ. Medical College, New York City.* Cobalt polycythemia was produced in 15 normal adult rabbits by the daily subcutaneous injection of 7 mgm. of cobalt as cobaltous sulfate and 3 mgm. of manganese as manganous chloride for an average period of 25 days. The initial hemoglobin level averaged 10.7 gms. and increased to 14.7 grams with a corresponding average increase in red blood cells from 5.1 Million to 7.7 Million.

Three possible mechanisms of the cobalt effect were investigated: 1. Neural mechanism. Cobalt administration to animals with a denervated hind limb produced tibial marrow in the denervated limb identical by smear counts, degree of hyperplasia, and respiration and glycolysis studies to that of the opposite undenervated limb. In contrast to Davis's concept of a local neural mechanism, (J. Pharmacol. and exper. Therap. 70: 408, 1940) this evidence indicates that the peripheral innervation of the marrow plays no role in the process.

2. Histological changes in the marrow blood vessels. No structural changes in the marrow blood vessels comparable to those observed in polycythemia vera (Reznikoff, Foote and Bethea, Am. J. Med. Sci. 189: 753, 1935) were found.

3. Chemical depression of bone marrow respiration and glycolysis. The respiration and glycolysis of cobalt polycythemic marrow were unaltered in comparison to those of hyperplastic marrows produced by other means. Furthermore, in vitro addition of cobalt to normal marrow caused no significant change in respiration or glycolysis. [*Aided by a grant from the John and Mary R. Markle Foundation.*]

Post-operative hemoglobin and plasma protein values. BENJAMIN WHITE SEAMAN (by invitation) and ERIC PONDER. *The Nassau Hospital, Mineola, N. Y.* After major surgical procedures in man, the post-operative fall in hemoglobin concentration follows a regular curvilinear course over a period of from 2 to 4 days when complications are absent, but the extent of the fall is often much greater than would be expected on the basis of the amount of blood lost at operation. The explanation suggested for this is that there is a post-operative inhibition of hemapoiesis, although changes in vascular volume and even hemolytic processes may contribute to the result.

After partial gastrectomy, partial colon resection, and other major surgical procedures, the plasma protein concentration falls to a much greater extent than would be expected from the amount of blood lost at operation. It is suggested that this post-operative fall in plasma protein concentration is largely due to a disturbance of the physiological mechanism which maintains the protein concentration in its steady state, and that this disturbance bears a relation to the inhibition of hemapoiesis which occurs at about the same time. Meanwhile, we suppose that these effects follow on tissue damage, and there is a certain amount of indirect evidence to support this belief.

The isolated head of the young animal as a test preparation for studying the periodic discharges of the respiratory center. W. A. SELLE. *Dept. of Physiology, Univ. of Texas, School of Medicine, Galveston.* It was previously reported that the respiratory center of the young animal is much more resistant to anoxia than is that of the adult and that survival of gasping of the isolated ischemic head is inversely proportional to age for animals up to or slightly past the period of weaning.

The present study indicates that the isolated head of a young animal, such as the rat, can be used successfully as a test preparation for studying the effect of drugs on the periodic discharge of the respiratory center. Using a technique previously described, a large number of chemical agents (92), varying widely in composition and action, were injecte dsubcutaneously or intraperitoneally into 12 to 15 day old rats. In case of volatile agents, the animals were subjected to the vapors in anaesthetizing chambers. Following intervals ranging from three minutes to several hours, or even days, depending upon the rapidity of action of the test material, the head was quickly isolated. The gasps resulting were mechanically recorded; in some instances action currents of the brain stem were also recorded. Most of the drugs tried had little or no effect on the nature or character of the gasping pattern or on the total duration of gasping. The following agents, however, definitely reduced the survival time of the center: iodoacetic acid, thyroxin, dinitrophenol, ether, chloroform and hypnotics of the barbituric acid series. In proper dosage the following prolonged survival: morphine, alcohol, urethane, and cyclopropane. Several preparations of chloralose were very effective in increasing survival; others were ineffective.

The pathology of desoxycorticosterone overdosage in various species. HANS SELYE and C. E. HALL (by invitation). *Dept. of Anatomy, McGill Univ., Montreal, Canada.* The characteristic morphological and functional changes caused by overdosage with desoxycorticosterone acetate (D.C.A.), a synthetic corticoid hormone, have been studied in the dog, monkey and rat. It has been found that none of these species develop any marked degree of water retention or tissue edema even if enormous doses are given (40 mg /day for small dogs or monkeys and 10 mg./day for the rat) over a period of several weeks or months. Even simultaneous treatment with large doses of NaCl failed to cause significant water retention in any of these species. On the other hand, severe motor disturbances which may progress to complete paralysis and death, result

in all these species if NaCl is administered following pretreatment with such high doses of D.C.A. Withdrawal of the NaCl causes the motor disturbances to disappear in spite of continued D.C.A. administration. The possibility of correlations between these motor disturbances and the anesthetic effect of D.C.A. and other steroids has been emphasized.

The kidneys showed varying degrees of tubular hypertrophy and glomerular sclerosis, while the adrenal cortex and medulla exhibited signs of marked involution in the D.C.A. treated animals. [*Work performed during the tenure of a Canadian National Research Council Studentship.*]

Improved peripheral resistance for the circulation schema. HERBERT SHAPIRO. *Dept. of Physiology, Hahnemann Medical College, Philadelphia.* In the Schema of the Circulation described in detail in Bard-Macleod's *Physiology in Modern Medicine* (p. 412, 9th ed., 1941) the "peripheral resistance" takes the form of 5 glass tube outlets packed with heavy pipe cleaner wicks. Four of these are adjusted for an outflow of 2 drops per second, the fifth for 1 drop per second. These wicks have certain disadvantages, of which the most important are (1) they cannot all easily be made of the same value of resistance (2) time is wasted in adjusting each tube until it has the proper resistance (3) during the experiment the value of the resistance may vary, owing to swelling of the wicks. By replacing the wicks with Pyrex capillary tubing (bore 0.3 mm), these disadvantages may be circumvented. Four of these capillaries are cut to a length of 19 mm, and the fifth is 38 mm long. As used in the physiology course in this laboratory, the capillaries have proven entirely satisfactory in saving the student's time, and facilitating the use of the schema by providing resistances whose values are maintained at a constant level. It is also easier to observe the flow directly from the outlet. The amount of clogging encountered is small.

A new method for determining relative tension and resilience of human muscles. M. L. SILVER (by invitation), GEORGE B. BEAN (by invitation) and ARTHUR H. STEINHAUS. *George Williams College Laboratory for Physiologic Research in Physical Education, Chicago.* Although employing electrical equipment, this method does not require recording of muscle potentials. Our apparatus employs the same principle as does the stimulator-vibrator described by Brown and Yacorzynski (Arch. Neurol. and Psych. 47: 813, 1942).

A disc of 1 sq. cm. area, firmly attached to the end of an arm that vibrates in the field of an electromagnet, rests with a known weight on the skin over a muscle. The electromagnet, from a compact Utah loudspeaker unit, is driven by a sine-wave generator with sufficient power to produce maximum deflection at frequencies from 1 to 1,000 cycles per second. The amplitude of excursion of the vibrating head is controlled by a potentiometer in the output circuit of the generator, and permits lateral movements up to 2 mms, with a sensitivity of 1μ

The actual amplitude of excursion of the vibrating head under varying conditions is determined from the voltage generated by torsion of a piezo-crystal (standard phonograph crystal cartridge, Shure Bros. type 42A) connected through an aluminum bar to the vibrating head. This voltage is amplified and applied to a standard output meter that has been calibrated in microns by stroboscopic observation of the vibrating head.

In an experiment, the driving power of the magnetic unit remains constant. The frequency of vibration is gradually increased while the amplitude of excursion is observed on the output meter. The frequency at the point of maximum excursion is taken to be the frequency at which the muscle is in resonance with the applied vibration, i.e., the *resonant frequency*, and as such is indicative of its tension. The amplitude of movement of the vibrating head is taken as a measure of the muscle *resilience*.

Some observations on tension and resilience in stretched and contracted human muscles. M. L. SILVER (by invitation), ALBERT KELSO (by invitation) and ARTHUR H. STEINHAUS. *George Williams College Laby. for Physiologic Research in Physical Education, Chicago.* Employing the resonant frequency method previously described, a series of observations on the biceps brachii of five normal adult subjects indicates an average resonant vibration frequency of 126 $\pm$ 2 cycles per second for the relaxed muscle. During passive stretching this was increased to 155/sec. in increments roughly proportional to the weights used to produce strength. During active contraction the resonant vibration frequency was increased to 144/sec. At these resonant frequencies, and with a constant driving power, relaxed muscles permitted the vibrating head to move 94μ, passively stretched muscles permitted only 60μ, and actively contracted muscles permitted an average movement of 128μ. Although these figures have only relative significance, they indicate that increasing muscle tension, no matter what its cause, increases its resonant frequency. And that when the increased tension is due to passive stretching, the resilience of the muscle is *reduced* (av. 38%) whereas when tension is due to contraction the resilience is *increased* (av. 36%). This latter observation, the only one that is unexpected from a purely physical standpoint, is taken to reflect some change in the colloidal state of the contracting muscle.

If resilience, as experimentally defined above, is

the equivalent of the elasticity coefficient described for frog sartorius by Gasser and Hill (Proc. Roy. Soc. 96: series B; 398, 1924) using purely mechanical recording apparatus, then this paper confirms their observation that contracting muscle is more elastic than resting muscle.

Effect of temperature on urine and phenolsulphonphthalein excretion of white rats at high altitudes. HERBERT SILVETTE. *Dept. of Pharmacology, Univ. of Virginia, Charlottesville.* Groups of 12 white rats in individual urine-metabolism cages were subjected to a simulated altitude of 15,000 feet (428 mm. Hg) in a low-pressure chamber of 500 liters capacity maintained at a constant temperature of 10°, 20° or 30°C. At the start of the 3-hour metabolism period the animals (weighing about 250 grams) were injected intraperitoneally with 5 cc. per 100 grams of a solution containing 0.2 per cent NaCl and 2 mgm. per cent phenolsulphonphthalein, and at the end of the period the collected urine was measured and the dye concentration determined colorimetrically. The following table gives the average 3-hour excretion of urine and phenolsulphonphthalein in percentages of the injected fluid and dye (36 animals in each series; probable error of averages from ±0.9 to ±2.8):

Temperature	0 feet		15,000 feet	
	Urine	P.S.P.	Urine	P.S.P.
10°	74	66	94	65
20°	54	64	80	70
30°	42	55	74	61

It will be seen that, regardless of the temperature employed, the animals reacted to 15,000 feet equivalent altitude with polyuria, which was further increased by cold but decreased by warmth. The fact that the simultaneous excretion of phenolsulphonphthalein was not significantly affected appears to be an indication that, in the slight degree of renal anoxia produced by 3-hour exposure to an altitude of 15,000 feet, the secretory function of the renal tubule remained unaffected, while the reabsorptive faculty of the tubule cells was partially inhibited, thus leading to polyuria with normal dye excretion. [*This investigation has been made with the assistance of a grant from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.*]

The influence of muscular work and fatigue on the state of the central nervous system. ERNST SIMONSON, NORBERT ENZER (by invitation) and ROY BENTON (by invitation). *Research Laby. of Mt. Sinai Hospital and the Northwestern Mutual Life Insurance Company, Milwaukee, Wis.* The fusion frequency of flicker, which earlier investigations have revealed to be a sensitive index of the state of the central nervous system in various physiological and pathological conditions, was investigated in 54 normal subjects (29 men, 25 women) between 18 and 40 years, before and after four different types of exercise of increasing severity (static exercise, 30 genuflexions, pulley exercise for three minutes or until fatigue, running until fatigue). Each exercise produced definite deviations of the fusion frequency. The majority of normal people (85 and 90%) respond with an *increase* of the fusion frequency after static exercise and 30 genuflexions, and with a *decrease* (96 per cent) after running. The different response between moderate and hard exercise is statistically highly significant. After pulley exercise, about 40 per cent of the subjects respond with both increase and decrease. The magnitude and the duration of the depression corresponds to the severity of exercise. These results may explain the depressing effect on the state of the central nervous system of physical fatigue after severe muscular exercise, and the stimulating effect of short, moderate exercise. The endurance of women in static exercise, pulley exercise, and running is significantly lower than that of men, while there is no significant difference in the reaction of the fusion frequency of flicker. The response of the fusion frequency of women after an equal amount of work (30 genuflexions) appears to be less than that of men.

A fifth cranial nerve projection to the cerebellum. RAY S. SNIDER (introduced by Philip Bard). *Dept. of Physiology, the Johns Hopkins Univ. School of Medicine, Baltimore, Md.* Surface positive potentials were recorded from the cerebellum of the cat when (1) branches of the fifth nerve were stimulated electrically and (2) when hairs, located in the field of distribution of the fifth nerve, were lightly activated by a mechanically vibrating artist's brush. Tactile stimulation by the latter procedure gave well localized potentials in the postero-medial part of the anterior lobe and anterior two folia of the lobulus simplex. The latency of the responses was 10–14 msec. They were predominately ipsilateral and were abolished by unilateral section of the fifth nerve. Occasionally, similar potentials were recorded from the ipsilateral paramedian lobule and medial folia of Crus I and Crus II.

With electrical stimulation of the major branches of the fifth nerve, it was not possible to obtain evidence of localization in the anterior lobe; responses were recorded in the culmen, I. centralis, I. simplex, tuber vermis, pyramis, and ansoparamedian lobule. Ipsilateral responses were always larger and easier to elicit than contralateral ones. The latencies average 2 msec. shorter than those obtained by tactile stimulation.

Factors affecting the survival time of isolated frog muscle. C. R. SPEALMAN. *Dept. of Physiology, Medical College of Virginia, Richmond.* A preliminary study of factors affecting the survival time of isolated frog mtscle under the nonsterile and otherwise unphysiologic conditions which prevail in ordinary laborotory practice was made. Two types of preparation were used: the frog heart, perfused by way of the sinus venosus, and the sartorius muscle, maintained in a shallow, frequently-changed bath of Ringer's solution. The effect of modifying the composition of Ringer's solution, of the addition of Mg, phosphate, glucose, creatine, and lactic acid either singly or in combination, of varying the work output of the heart, and of temperature were studied. The endpoint of survival in the case of the sartorius muscle was complete inexcitability to electrical stimulation. With the heart, the appearance of persistent block and (in separate experiments) the rate of decrease in amplitude of contraction (heart electrically driven) were used as indicators of the survival time.

Several modifications of Ringer's solution did not influence the survival time of the frog sartorius muscle. The heart generally survived in good functional condition longer when Mg ion was added to Ringer's solution; further addition of phosphate seemed to be beneficial. The other modifications of Ringer's solution which were tested were without effect or were deleterious; work output did not appear to be an important factor. Total survival time of the sartorius muscle and the time of survival of the heart in good functional condition were considerably decreased as the temperature increased.

Galvanic and faradic stimulation of the labyrinth (site of action and mechanism). E. A. SPIEGEL and N. P. SCALA (by invitation). *Dept. of Experimental Neurology, Temple Univ. Medical School, Philadelphia, Pa.* On electric stimulation of the vestibular apparatus (monaural or binaural stimulation) typical responses are still obtained after destruction of the peripheral sense organ, while intracranial section of the 8th nerve prevents such reactions. It is concluded that the electric stimulus acts upon the peripheral neuron. Faradic stimulation of the vestibular nerve, while unable to elicit definite nystagmus, may produce a one-phasic reflex response such as a rotation of the head to the opposite side (contralateral cephalogyric reaction). Thus the doctrine of unexcitability of the vestibular nerve by faradic current cannot be maintained. The chronaxie of the vestibular nerve was determined, the contralateral cephalogyric reaction serving as criterion (liminal response); values from 0.9–1.8 milliamperes were obtained. In an attempt to ascertain the mechanism of the inverse effects of anodic and cathodic stimulation no evidence could be obtained indicating that this phenomenon is due to quantitative differences in the action of the two poles upon two antagonistic sets of vestibular fibers. A depressor action of the anode upon the receptors of the semicircular canals could also be excluded. However, a depressor action of the anode limited to tonic labyrinthine impulses could be observed which may be responsible for the inverse effect of anodic and cathodic stimulation.

Anticonvulsant effects of desoxycorticosterone, testosterone and progesterone. E. SPIEGEL. *Dept. of Experimental Neurology, Temple Univ. School of Medicine, Philadelphia, Pa.* Continuing studies with Wycis on hypercholesteremia, it was ascertained whether steroids influence the convulsive reactivity. This was expected in view of the influence of desoxycorticosterone upon cellular permeability, and Selye's observation of anesthetic effects. While experiments on rabbits (with Silverstein) were negative, an increase of the convulsion-threshold on electric stimulation with the skull intact and/or a diminution of the duration of the seizures was observed in white female rats of about 100 grams on intraperitoneal injection of 24–33 mgm. desoxycorticosterone acetate (5 mgm. per cc. sesame oil) or with 2.5–4.0 mgm. of more concentrated solutions (15 mgm. per cc. cod liver oil). These changes of convulsive reactivity appeared when motility and reactivity to painful stimuli were only slightly diminished. The dose producing loss of spontaneous movements and eventually respiratory failure lies, however, rather close (lethal dose: 4–6 mgm. of the concentrated solution per 100 grams in females). In male rats much higher doses (36 mgm. and more in concentrated solution per 100 grams body weight) were necessary to reduce the convulsive reactivity. Similar results were obtained with progesterone and testosterone. Intraperitoneal injection of 6–7 mgm. progesterone (12.5 mgm. per cc. sesame oil) per 100 grams (female rats) reduced the convulsive reactivity; the lethal dose was 9–12 mgm. Using testosterone (25 mgm. per cc. sesame oil) the anticonvulsant dose was 17–26 mgm. in female rats, the lethal dose 20–40 mgm. per 100 grams. [*Aided by a grant from the Schering Corp. through the courtesy of Dr. Ed. Henderson.*]

Improvement of muscular co-ordination and visual functions by cold hip baths. ARTHUR H. STEINHAUS and ALBERT KELSO (by invitation). *George Williams College Laby. for Physiologic Research in Physical Education, Chicago.* Shortly after breakfast the subjects (males 17–45 yrs.) were put through a series of tests. On *experimental* days the cold hip bath followed immediately. About 2½ hours later the tests were repeated. On *control* days tests were given on the same time

schedule without a bath. A total of 37 subjects were studied.

The self-administered hip bath is taken seated with feet on a second stool, thighs and legs flexed. From a shower head connected by flexible hose to a mixing valve, the lower abdomen (umbilicus to groin) is sprayed 3–5 minutes with increasingly hotter water followed by gradual change to tap coldness (45°–65°F.) maintained 5–15 minutes. Overall time never exceeds 20 minutes. Each subject's comfort dictates extremes of temperature and speed of change. Symptoms of slight cramps or discomfort terminate the cold period.

Ninety-seven experimental compared with 87 control days disclosed improvement of 5 per cent in tapping rate and 8.6 per cent and 8.3 per cent in two different eye to leg muscle reaction time tests. Lateral visual imbalance as determined by Telebinocular Service on 69 experimental and 84 control days averaged 11.9 per cent improvement. Visual acuity by Telebinocular, left and right eyes separately, (160 experimental, 194 control) averaged 17 per cent improvement. In a smaller group (predominately 20–20 vision) tested by the Ferree-Rand broken circle modification of the Snellen Chart, acuity improved 11.4 per cent. his same group showed only 10.2 per cent improvement on the Telebinocular scale. Rate of flicker fusion tested by oscilloscope improved 16.2 per cent, by the Simonson and Enzer rotating disc method (48 experimental, 49 control) improved 9.3 per cent. All of these improvements are statistically significant.

Blood studies on dogs exposed to discontinuous anoxia. J. Clifford Stickney (by invitation) and David W. Northup. *Dept. of Physiology, School of Medicine, West Virginia Univ., Morgantown.* After a preliminary control period, 5 dogs weighing 7.83 to 11.92 kilograms were exposed for 8 hours daily (except Sundays) by means of a low pressure chamber to a stimulated altitude of 18,000 feet for a period of 88 days.

Weekly, during the control and experimental periods, the blood specific gravity was determined on freshly drawn samples of venous blood by the falling drop method of Barbour and Hamilton. Hemoglobin was determined by the Sahli method, and red blood cell counts were made with the improved Neubauer counting chamber. At monthly intervals plasma protein was determined on 3 of the dogs by a modification of the method of Guillaumin, Wohl and Laurencin. Red blood cell fragility tests were made at the conclusion of the experimental period.

The average blood specific gravity increased from 1.0569 to 1.0719 during the period of exposure to discontinuous anoxia. Hemoglobin values increased 53 per cent while the number of red blood cells increased 67 per cent on the average. The fragility of the red blood cells was normal; hemolysis began at 0.46 and was complete at 0.33 per cent NaCl.

The average plasma protein value decreased from 6.77 to 6.11 grams per 100 cc. of plasma, but the difference is not statistically significant. In one dog there was an increase after the first month and a decrease after the third month. In two dogs there was a persistent decrease; in but one was this statistically significant throughout.

Mechanism of erythremia following intravenous adrenalin in human beings and dogs and in traumatic shock in dogs. Robert D. Taylor (by invitation) and Irvine H. Page. *Lilly Laboratory for Clinical Research, Indianapolis City Hospital, Indianapolis, Ind.* Shock due to partially occluding limb tourniquets (pentobarbital anesthesia) produced 70 per cent less erythremia (rise of hematocrit index) than developed in 15 normal dogs. This effect of splenectomy was mimicked in lesser degree by intravenous infusion of F 933; in these as in splenectomized dogs, the decreased erythremia was due to elimination of the rise occurring in the first hour of experiments in normal dogs. Similarly, the erythremia of shock due to intestinal manipulation was reduced by 50 per cent in 10 splenectomized dogs as compared with 10 controls.

Prevention of local fluid loss by application of plaster limb casts before tightening the tourniquets abolished any rise in hematocrit in four splenectomized dogs and four dogs infused with F 933 but not in six normal dogs.

The differences between normal dogs, and those which had been splenectomized or treated with F 933 are attributed to elimination or inhibition of splenic contraction with discharge of highly cellular blood. Testing this, adrenalin given intravenously to six normal dogs and, in much lesser degree, in six normal human beings, produced an erythremia similar to that occurring initially in shock. Adrenalin caused no erythremia in six splenectomized human beings.

A large proportion of the erythremia of shock in dogs as measured by hematocrit is therefore due to splenic discharge of cells rather than to fluid loss. The residual erythremia is due to local loss of fluid. The concepts of a generalized increased capillary permeability or sequestration of plasma in shock produced by tourniquets or intestinal manipulation are not supported.

Factors influencing the antithromboplastin content of normal and hemophilic plasmas. Leandro M. Tocantins. *Division of Hematology, Dept. of Medicine, Jefferson Medical College, Philadelphia.* Normal plasma separated from blood and rendered "cell free" within 5 minutes of its collection, without anticoagulants, remains fluid and retains its antithromboplastin activity for several hours.

Hemophilic plasma, under similar conditions, has remained fluid and maintained its antithromboplastin activity for 4 days. Antithromboplastin in "platelet free" citrated plasma may be detected in reduced amounts, or not at all, following: a, over-recalcification of the plasma beyond the amount required to produce a minimal clotting time (under-recalcification exaggerates antithromboplastin activity); b, exposure to a pH below 5 or above 9; c, filtration through a coarse (V) Berkefeld candle; d, incubation with 0.1 volume of colloidal $Mg(OH)_2$; e, exposure to tissue juices or to the products of platelet disintegration.

Plasma globulin fractions precipitated by dilution and acidification display some antithromboplastin activity, which may be marked if the fraction is obtained from hemophilic plasma, and diminished or absent if obtained from heated (65° C for 5') plasma, or plasma to which a small amount of dilute tissue extract has been added.

Antithromboplastin is impotent against the thromboplastin-like action of dilute solutions of Russell viper venom. This may explain why the venom acts with equal effectiveness on normal and hemophilic plasmas.

Failure to demonstrate vagus fibers in the splanchnic nerves in dogs. J. EARL THOMAS and BERNARD J. ALPERS (by invitation). *Dept. of Physiology and Neurology, Jefferson Medical College of Philadelphia.* According to Iwama numerous vagus fibers join the sympathetic trunk at the level of the inferior cervical ganglion and are ultimately distributed via the splanchnic nerves in cats. Rasmussen and Duncan (Proc. Soc. Exper. Biol. and Med. 23: 794, 1925) were unable to confirm Iwama's results in cats or rabbits. We were led to investigate the situation in dogs because of the known presence in the dog's splanchnic of cholinergic secretory fibers for the pancreas. The right vagus nerve was cut in the neck under aseptic condition in 3 dogs and the left vagus in 2 dogs. After a lapse of from 14 to 16 days both splanchnic nerves and parts of both vagus nerves were excised and fixed in 10 per cent formalin. These were studied by serial sections by means of the Marchi stain and the Bodian stain. Sample sections were stained by Hematoxylin Eosin and the Gros-Bielschowsky method. All stains were controlled by normal nerve tissue from the unoperated vagus nerve. In one dog (dog 3) a single axis cylinder in the splanchnic nerve on the operated side was found to be swollen and bulbous. In another animal (dog 1) two such axis cylinders were found. These were demonstrated in only one section and were not found subsequently. All other splanchnic axis cylinders both in these and other animals were normal. The Marchi stain revealed no evidence of myelin degeneration. No evidence of inflammatory change was found in any of the specimens.

The findings were interpreted to indicate that there appear to be no fibers contributed by the vagus to the splanchnic nerve of the dog.

The electroencephalogram during mental effort. J. E. P. TOMAN (introduced by Robert H. Oster). *Dept. of Physiology, Univ. of Maryland School of Medicine, Baltimore.* Electroencephalograms of 64 medical students were recorded during the calculation of an arithmetical progression and during relaxation. Mean percent-time-alpha was 54.4 at rest and 48.2 during mental effort. The significance of the difference in means could not be established because of the wide scatter in percent-time-alpha among individuals. 43 subjects showed some decrease, 12 showed some increase, and 9 showed no change during mental effort. Where measured, amplitude of alpha rhythm was reduced in 11 subjects, increased in one case, unchanged in 7 cases. Of 33 subjects who signalled each answer, there was no correlation between problem cycle and E. E. G. in 31 cases, doubtful correlation in 2 cases. It is concluded that mental arithmetic is not accompanied by marked or consistent changes in the electroencephalogram.

All subjects with good alpha rhythm showed typical blocking by dim pattern vision, followed in 34 cases by a rebound above normal in amplitude and regularity of alpha rhythm. Sound, particularly air-blast, temporarily blocked the alpha rhythm, but only if the subject was unprepared for the stimulus. In three subjects from whom visual flicker potentials were elicited it was not found possible to drive the cortical rhythm by sound clicks of the same frequency range. [*Supported by a grant from the Bressler Alumni Research Fund.*]

Effect of hormones on the sensitivity of striated muscle and on the activity of choline esterase. CLARA TORDA (introduced by Harold G. Wolff). *Dept. of Medicine (Neurology), Cornell Univ. Medical College, New York City.* While sex hormones and some of the hormones secreted by the hypophysis do not contract the striated muscle in low concentrations, they may modify the biochemical equilibrium of the muscle. An investigation of the acetylcholine and potassium sensitivity of the rectus abdominis muscle of frog and the activity of the choline esterase of brain tissue (method of Bernheim and Bernheim and method of Warburg and Ammon) showed that Follutein (anterior pituitary like sex hormone, Squibb), progestin (corpus luteum hormone, Roche-Organon), Estrone Suspension (follicular hormone, Abbott), Testosterone Propionate (Schering) and Pitressin (oxytocic principle of the posterior part of the hypophysis, Parke-Davis) potentiate the action of the striated muscle to acetyl

potassium and depress the activity of choline esterase. Pitocin (anti-diuretic hormone of the posterior part of hypophysis, Parke-Davis) does not change the sensitivity of the striated muscle or the activity of choline esterase.

These results suggest that the above mentioned hormones participate in the maintenance of the threshold of excitability of the effector cells.

Effect of low pressures on the weights of endocrine organs, spleen and kidney in rats. FRANK J. TORNETTA (by invitation), ALBERT S. GORDON, SAVINO A. D'ANGELO (by invitation) and HARRY A. CHARIPPER. *Dept. of Biology, Washington Square College of Arts and Science, New York Univ., New York City.* Forty seven adult male rats (210–280 gms.) were exposed to pressures of 250–280 mm. Hg (25–28,000 ft.) 6 hrs./day for 14–18 days. Significant increases in the weights of adrenals and decreases in testes, seminal vesicles, prostates, thyroids, thymi, and kidneys were noted when compared with similar organs in 44 control rats. Weights of the pituitary and spleen were not affected significantly by this treatment. Body weight loss in the experimental animals ranged only from about 10 to 15 per cent and was not responsible for the endocrine gland weight changes.

Fifty-eight adult male rats were given 18–20 hr./day exposures to the same pressures for 3–12 days. Body weight losses in these animals were considerable and ranged from about 15 to 30 per cent despite the fact that food was always available. Increases in adrenal and decreases in testis weights were also observed in this group but they were not as marked as those occurring in the discontinuously-exposed animals. In the animals given long daily exposures, considerably greater decreases were noted for thyroid, thymus and kidney; spleen and pituitary also diminished in weight. It is difficult to interpret the organ weight changes in the animals given these long exposures since the effects of anoxia are complicated by those of the chronic inanition. It would appear that the animal subjected to low pressures daily for relatively short times (6 hrs./day) is better suited for studies of the effects of anoxia on endocrine organ activity.

Some effects of protein-deficient high-fat diet upon dogs. TSAN-WEN LI (by invitation), VICTOR H. HOUGH (by invitation), E. P. MONAHAN (by invitation) and SMITH FREEMAN. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* Seven normal adult dogs were fed 40 calories/lb. of a protein-deficient, high-fat diet (lard 33, sucrose 55, yeast 5, cellophane 5, salt 2, with 10 drops percomorphum oil per kilogram of diet).

An additional 5 dogs were kept on an iso-caloric diet in which 25 per cent of casein was fed in place of sugar.

The deficient animals lost appetite and weight after 3–8 weeks. They became anemic and developed trophic ulcers on extremities. They survived 12–18 weeks. Three of them were found at autopsy to have chronic duodenal ulcers. The control animals remained healthy and active throughout and were sacrificed after 16 weeks.

The following determinations were carried out every two weeks: phosphatase, total fatty acids and cholesterol upon the fasting serum; also hepatic clearance of Rose Bengal. The total fat and cholesterol content of livers were determined. The following changes were found in the deficient animals:

1. Definite elevation of serum fatty acids (152–662 mgm. per cent above initial) and cholesterol (30–370 mgm. per cent).

2. Significant increase in serum phosphatase (9.3–82.5 units from initial) and significant drop in dye clearance (56–102 per cent).

3. Some enlargement of liver (ave. 13.0 grams per lb. body weight as compared to 11.2 grams in the controls).

4. Increased liver lipids (ave. 18.5 per cent, or 2.8 grams fat per lb. body weight as compared to 6.1 per cent, or 0.7 gram in the controls).

5. The fat increase in the liver was largely made up of neutral fat.

Effects of added cholesterol on dogs fed with protein-deficient, high-fat diet. TSAN-WEN LI (by invitation), VICTOR H. HOUGH (by invitation), E. P. MONAHAN (by invitation) and SMITH FREEMAN. *Dept. of Physiology, Northwestern Univ. Medical School, Chicago.* Eleven dogs were fed a protein-deficient, high-fat diet and were treated in the same way as in the preceding communication, but in addition, cholesterol was administered with the food in daily doses of 0.1 gram per lb. of body weight. Loss of appetite and weight, development of anemia, hypoproteinemia and trophic ulcers and the survival period were similar to the animals without cholesterol. Six had chronic duodenal ulcers.

The effects of added cholesterol upon protein deficiency are:

1. Cholesterol exaggerates the elevation of fatty acid and cholesterol in serum (225–1771 and 172–1251 mgm. per cent above initial respectively).

2. Maximum alteration of serum phosphatase and liver function is not very significantly different.

3. Cholesterol causes a sharp drop in dye clearance at the end of 2 weeks (lowest, 38 per cent), and the change is significant even after 4 days of feeding (88–61 per cent). Usually the clearance increases to a higher sub-normal value later.

4. Livers were definitely enlarged (average 15 grams per lb. body weight).

5 The amount of fat deposited was double with

cholesterol feeding (average 25.7 per cent, or 6.2 grams per lb. body weight).

6. Cholesterol in the liver increases proportionately more and thus it increases cholesterol to fat ratio (6.2 per cent).

Four additional dogs kept on high-fat, complete diet (25 per cent casein) with cholesterol were sacrificed after 16 weeks. Elevation of serum lipoids was much less. The livers were of normal size, and with one exception not fatty. There was little or no change in the liver function and serum phosphatase.

The effect of anoxia on peristalsis of the small intestine. EDWARD J. VAN LIERE, DAVID W. NORTHUP, J. CLIFFORD STICKNEY (by invitation) and GEORGE A. EMERSON (by invitation). *Depts. of Physiology and Pharmacology, School of Medicine, West Virginia Univ., Morgantown.* The intestinal activity of mice was studied by a modification of Macht's technique. The material placed into the stomach consisted of 10 per cent powdered charcoal and 10 per cent gum acacia in water. Mice in groups of five were intubated and ten minutes later placed into a low pressure chamber. The chamber was constructed to provide adequate ventilation so there was no accumulation of carbon dioxide.

Twenty mice were subjected to a partial pressure of oxygen of 94 mm. Hg; twenty-five to 80 mm. Hg and the same number to 48 mm. Hg. These partial pressures correspond approximately to altitudes of 14,000, 18,000 and 30,000 feet respectively. In each instance the same number of animals were used. The mice were sacrificed at the end of forty minutes and the distance the charcoal had traversed the small intestine was measured.

The intestinal activity as ascertained by this method in the mice subjected to a partial pressure of 94 mm. Hg showed no significant change from that of the controls. Those exposed to a partial pressure of 80 mm. Hg showed a statistically significant decrease in intestinal activity and those exposed to a partial pressure of 48 mm. Hg showed a still greater decrease. More severe grades of anoxia were not employed. It was concluded that the threshold lay between 94 and 80 mm. Hg and that the more severe the degree of anoxia the greater the decrease in intestinal activity. The work is being repeated on dogs

Hydroureter of pregnancy in the monkey. G VAN WAGENEN and RALPH H JENKINS (by invitation). *Yale Univ. School of Medicine, New Haven, Conn.* In an earlier paper it was shown that ureteral dilatation occurs during the later months of pregnancy in the rhesus monkey just as it does in the human. It is associated primarily with the presence of the placenta and persists, or can arise even as late as two months after the removal of the fetus if the placenta remains in place and functional. The dilatation, now, has been studied in two to four successive pregnancies beginning with a known first pregnancy. It is concluded that, although there may be a slight residual increase in size of the ureter after one pregnancy, there appears to be no definite progressive injury to the ureter as a result of repeated gestation *per se*. Further, in the healthy animal the maximum dilatation occurs in the first pregnancy and there is a decrease of dilatation in each succeeding pregnancy.

Electrocortical activity in cats with mesencephalic transections. V. C. VAUGHAN, III, and A. A. P. LEÃO (introduced by H. Davis). *Dept. of Physiology, Harvard Medical School, Boston, Mass.* Bremer has reported (1935 and subsequently) that cats subjected to transection of the cerebrospinal axis at the level of the colliculi have cortical electrograms characteristic of sleep. Since Bremer's recording technique probably precluded demonstration of the slow (delta) component of the electroencephalogram of sleep, it seemed worthwhile to repeat his experiments, using adequate amplifiers and an ink-writing oscillograph. We have been able to confirm Bremer's description of the mesencephalic transection preparation in every way, and have also found slow waves along with the "spindles" of 14 per sec. waves which he described. Some animals were transected through a sub-tentorial approach, leaving the scalp and skull intact over the cortex. Records taken through the intact scalp and skull showed the same features as those obtained directly from the pia and were closely similar to those obtained from intact sleeping cats with the same arrangement of electrodes.

The mesencephalic transection offers the opportunity of studying the electrophysiology of the cat cortex after the withdrawal of the ether under which the operation is performed, since the section itself produces anesthesia. The electrical response of the unanesthetized cortex to tetanic stimulation is identical with the *tonic-clonic sequence* described by Rosenblueth and Cannon.

Treatment of experimental renal hypertension with renal extracts containing renin. G. E. WAKERLIN, C. A. JOHNSON (by invitation), E. L. SMITH (by invitation), W. G. Moss (by invitation) and J. R. WEIR (by invitation). *Depts. of Physiology and Physiological Chemistry, Univ. of Illinois College of Medicine, Chicago.* We have already reported that daily intramuscular injections for four months or more of partially purified hog renal extract containing renin (in doses of 1 gram of renal cortex equivalent per kgm. of body weight) produced striking reductions in the blood pressures of renal hypertensive dogs, whereas heat-inactivated hog renin in 1 gram doses were without antihypertensive effects. There is continually increasing

evidence that these therapeutic effects are not due to antirenin.

We are now completing studies of the therapeutic effects of highly purified hog renin in 1 and 3 gram doses, partially purified heat-inactivated hog renin in 3 gram doses, partially purified dog renin in 3 gram doses and partially purified liver extract prepared after the manner of renin in 3 gram doses. The results suggest that the therapeutic effects of hog renal extracts containing renin are not due to renin but to some other substance or substances in the extracts, inasmuch as highly purified hog renin is less effective therapeutically than partially purified hog renin. The results confirm the ineffectiveness of partially purified dog renin. They suggest that the antipressor substance is partially heat-stable, inasmuch as heat-inactivated hog renin in 3 gram doses was moderately antihypertensive. The results also suggest that the therapeutic effects are specific for kidney since hog liver extract was ineffective. Work is in progress to clarify further the mechanisms involved, including the heterologous factor in the effectiveness of the renal extracts.

Treatment of spontaneous hypertension in the dog with hog renal extract containing renin. G. E. WAKERLIN, C. A. JOHNSON (by invitation) and B. GOMBERG (by invitation). *Depts. of Physiology and Physiological Chemistry, Univ. of Illinois College of Medicine, Chicago.* Direct mean, femoral artery blood pressure measurements on 200 comparatively young dogs revealed two moderately hypertensive animals. Sphygmomanometry on older dogs may show a higher incidence of hypertension.

During a control period of four months the blood pressures of one hypertensive dog ranged from 140–180 mm. Hg (average, 164) and those of the other animal from 130–170 mm. Hg (average, 148). The first dog was then injected intramuscularly with partially purified hog renal extract containing renin in a dose of 1 gram of fresh kidney cortex equivalent per Kg. of body weight daily for four months. There was a gradual decrease in blood pressure during treatment to 110–140 mm. Hg (average, 130). During the first three months following treatment the blood pressure gradually returned to the pretreatment hypertensive level of 140–170 mm. Hg (average, 152), where the pressures have remained for an additional six months. The second dog received the same treatment, except in a dose of 2 grams of renal cortex equivalent. The blood pressure gradually fell during therapy to 120–140 mm. Hg (average, 120). During the four months following therapy the pressures gradually returned to 140–160 mm. Hg (average, 154) where they have remained for two additional months.

No toxic effects were detected. Urinalyses, blood urea nitrogens, appetites, body weights, and general clinical conditions remained normal.

The results suggest that spontaneous (essential?) hypertension in the dog responds to partially purified hog renin similarly to experimental renal hypertension in this species.

Cortical auditory areas of the monkey as determined by electrical excitation of nerve fibers in the osseous spiral lamina and by click stimulation. EDWARD M. WALZL (by invitation) and CLINTON N. WOOLSEY. *Otological Research Laby. and Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* The type of study described for cat (Woolsey and Walzl, 1941; Bull. Johns Hopk. Hosp., Dec. 1942) has been extended to monkey. Single condenser discharges were delivered through fine wire electrodes to nerve fibers at the dissected edge of the osseous spiral lamina. Amplified contralateral and ipsilateral cortical responses were visualized oscillographically and photographed. The inferior and the superior banks of the Sylvian fissure were examined in opposite hemispheres. Finally, the auditory area was determined by click stimulation of the intact ear.

Both methods revealed that the auditory area occupies most of the inferior Sylvian bank from its caudal end to a level 4 to 6 mm. rostral to the caudal limit of the insula. Usually the area extends everywhere to within 1 mm. of the lip of the Sylvian fissure, while caudally it may spread over the lateral surface as far as the superior temporal sulcus. The area traverses the bottom of the posterior Sylvian fissure and extends for about 3 mm. onto the superior Sylvian bank posterior to the insula. The apex projects to the most rostral part, the middle turn to the region lateral to the posterior end of the insula and the basal coil to the remainder of the area. The evidence is insufficient to permit a statement regarding a "secondary" auditory area such as we have just described for the cat. However, the results indicate that the general deductions made (*loc. cit.*) regarding the homologies of the Sylvian fossa are valid.

Ischemia and possible toxic factors in shock. FRANK WARNER (introduced by L. B. Nice). *Chicago Medical School.* In 8 experiments with dogs "A" under ether anesthesia, the left hind limbs were traumatized by striking them 50 times with an iron pipe. These dogs went into shock within 2 to 6 hours with a great fall in blood pressure, hemoconcentration and swelling in the traumatized limbs.

A tourniquet was applied to these limbs just distal to the femur socket, excluding the artery and vein which were clamped and cannulated. The traumatized leg of each was amputated, weighed, and connected by rubber tubing to the central end of the cannulated femoral artery and

vein of the tourniqueted left hind limb of dogs "B" respectively; thus the blood of dog "B" perfused through the isolated leg of "A" and returned via the veins to "B" also under ether. Heparin was injected to prevent clotting. During the 14 to 29 minutes necessary to make connections the isolated limb was completely ischaemic. Blood pressure was recorded from a carotid artery.

A similar series of experiments was carried out without traumatizing the leg of dogs "A", but shock occurred in "B" in all these transfused cases. On reweighing the isolated limbs there was not a sufficient increase in weight to account for shock with great lowering in blood pressure and hemoconcentration in dog "B".

The ischaemia produced in the amputation of a traumatized or untraumatized leg may have caused toxic substances to form that were factors which helped cause the fall of blood pressure to shock levels.

The effect of potassium arsenite (Fowler's solution) on the respiration and glycolysis of normal and leukemic cells, with observations on the action of "synthetic vitamin K", menadione (2-methyl-1, 4-naphthoquinone). CHARLES O. WARREN. *Depts. of Anatomy and Physiology, Cornell Univ. Medical College, New York City.* Potassium arsenite, sometimes used clinically in the treatment of leukemia, depresses the respiration of normal and human bone marrow and human leukemic leukocytes to much the same extent. In these tissues, this is accompanied by an accumulation of lactic acid in contrast to the keto acid accumulation in liver and other tissues. An effort was made to find a substance which would protect normal but not leukemic cells from the action of arsenite. Menadione increases normal marrow respiration, decreases aerobic glycolysis and under selected conditions completely counteracts the effects of arsenite, at least for several hours. This "protective" action does not apply to liver or apparently to other tissues not normally exhibiting aerobic glycolysis. Mouse myeloid and lymphatic leukemia cells are not protected as well as normal rabbit bone marrow; human leukemic leucocytes were intermediate in this respect in a small series of cases. Neither succinate, citrate nor pyruvate overcomes the arsenite effect on marrow. Thionine and methylene blue, which have oxidation-reduction potentials similar to that of menadione, also partially counteract the arsenite effect on marrow. Menadione reacts with sulfhydryl groups (see abstract of Summerson); phthiocol does not and has no protective effect against arsenite. It remains to be determined whether the *in vitro* "protective" effects described here are applicable in the intact organism. [*Aided by a grant from the John and Mary R. Markle Foundation.*]

Effects of anoxia and hypoglycemia on the level of free acetylcholine in the cerebral cortex of the rat. J. H. WELSH (introduced by F. L. Hisaw). *Biological Laboratories, Harvard Univ.* Quastel *et al.* (1936) demonstrated that oxygen and glucose are important for the *in vitro* synthesis of acetylcholine (ACh) by brain slices. MacIntosh (1939) failed, however, to find a significant decrease in total ACh in the brains of mice killed in insulin convulsions. Likewise, Cortell, Feldman and Gellhorn (1941) concluded that anoxia and insulin hypoglycemia had no effect on the ACh content of the rabbit brain.

By extracting the free ACh, using cold, eserine-Ringer's solution, and by assay on two sensitive test preparations (isolated frog heart and Venus heart), it has been possible to demonstrate a marked effect of low barometric pressure and of insulin hypoglycemia on the cerebral cortex of the rat. Average values for free ACh in the normal rat were found to range between 0.26 and 0.68 gamma/gram of cortex in different series, employing different methods of extraction and assay. Subjecting rats to low barometric pressure for 1–2 hours produced a 40–50 per cent decrease in free ACh. A decrease was prevented by previous administration of prostigmine. Rats killed in insulin convulsions showed a loss in free ACh of 50–60 per cent.

Since other investigators have found the effects of hypoglycemia and anoxia on the electroencephalogram to be just the reverse of those produced by ACh, after an anti-cholinesterase, it is suggested that the well-known actions of low O_2 and glucose on the central nervous system are due, at least in part, to a decrease in the normal levels of ACh.

Parenteral use of aminoacids and gastrointestinal motility. K. WESTON (by invitation), M. J. OPPENHEIMER, N. LEARNER (by invitation) and H. STAUFFER (by invitation). *Temple Univ., School of Medicine, Philadelphia, Pa.* Parenteral use of casein hydrolysates in postoperative gastrointestinal surgery is increasing. Effects of intravenous aminoacids (Amigen, Mead Johnson) upon gastrointestinal motility of trained dogs and others anesthetized with morphine or pentothal-barbital, and of hospital patients (admitted for other than gastrointestinal complaints) were studied during slow (10–20 mgm/kgm/min) and fast (100–130 mgm/kgm/min or above) rates of injection. Balloon methods of recording were used.

Anesthetized dogs: Intestine (duodenum) tonus and amplitude unchanged during slow, both decreased during rapid injection. Duration of effects is short.

Trained Thiry-Vella and Biebl loop dogs: Motility (ileum) unchanged during slow injection. During fast infusion a period of preliminary stimulation is followed by one of longer inhibition.

Trained Pavlov gastric fistula dogs: Slow injec-

tion lowers tonus but does not influence hunger contractions. Emesis occurs with fast rates of injection.

Patients: Rapid injections produce abrupt decreases in tonus and disappearance of contractions. Latent periods and duration of effects are both short (minutes). Inhibition confirmed by X-ray, but was not always correlated with subjective symptoms. Inhibition occurred with blood levels as low as 6–7 mgm. aminoacid nitrogen/100 cc plasma; emesis at 11 mgm.

In dogs (trained or anesthetized) blood levels up to 10 mgm produced no changes in motility. Changes in blood pressure and respiration, pH, and volumes of injection were controlled in this study.

Antagonistic action of sensory stimulation to anesthetization. G. C. WICKWIRE (introduced by W. E. Burge). *Dept. of Physiology, Univ. of Illinois, Urbana.* Twenty-eight rabbits were each injected intravenously with 0.45 cc. of nembutal per kilogram of body weight. Fourteen of these rabbits were stimulated during the period of anesthetization with mild induction shocks from an inductorium by attaching one electrode to the hind leg and another to the ear. The time of recovery from the anesthetic in the stimulated and non-stimulated animals was noted. The animal was considered recovered from the anesthetic as soon as it could stand and walk.

The average recovery time of the unstimulated rabbits was 78 minutes while that of the stimulated group was 46 minutes, or a decrease of 41 per cent.

We have found (Am. J. Physiol. **116**: 1, 1936; Anesthesie et Analgesie **111**: 1, 1937; Anesthesia and Analgesia **20**: 2, 1941) that during anesthetization more negative charges left the brain by efferent nerves than came to it by afferent nerves, resulting in a loss of negative charges thereby decreasing the negative potential of the brain cortex with resulting decrease in irritability and anesthesia. During recovery from anesthesia, more negative charges came to the brain by afferent nerves than left by efferent nerves thereby increasing the negative potential of the brain cortex. This suggests that the reason the rabbits that were stimulated recovered more quickly from the nembutal was that the stimulation set up negative charges which passed to the brain cortex thereby increasing its negative potential with resulting increase in irritability and recovery from anesthesia.

Refinements in the Stewart method for determining cardiac output. HAROLD C. WIGGERS. *Dept. of Physiology, Western Reserve Univ. Medical School, Cleveland, O.* Stewart's salt-injection method (Am. J. Physiol. **57**: 27, 1921) for obtaining cardiac outputs in anesthetized dogs seems as reliable in principle as the Fick method. The inconsistent, high values reported by Stewart were probably related in part to the relatively crude technique employed. Following several technical refinements, consistent values have been repeatedly obtained. These improvements include the following: 1. For each animal a saline concentration and injection rate was determined which produced adequate conductivity changes without altering cardiac rhythm or strength of beat as judged from electrocardiograms and central arterial pulses. 2. Instead of employing both femoral arteries, blood was withdrawn from the same artery in which the presence of the injected salt was detected by unbalance of a Wheatstone Bridge. To this end, a special conductivity cannula was inserted between central and peripheral ends of a femoral artery, thus maintaining constant blood flow to that limb. When the injected salt reached maximal concentration in this cannula, 4 cc. of blood were rapidly withdrawn by a syringe via a side outlet. 3. The apparatus for electrotitration of blood samples for equivalent conductivities was materially improved by utilization of modern equipment and design of a conductivity cell permitting stirring of blood samples.

The method, thus modified, yields quite consistent values on repeated determinations. These compare favorably in most instances with simultaneous Fick determinations, but run somewhat higher. On the basis of experience, our Fick rather than our salt injection values were questioned when discrepancies arose.

Cardiac output and total peripheral resistance measurements in intact barbitalized dogs. HAROLD C. WIGGERS and KENNETH HUIZENGA (by invitation). *Dept. of Physiology, Western Reserve Univ. Medical School, Cleveland, O.* Cardiac outputs in 11 large (18–23.5 K.) and 4 medium-sized (10–12.5 K.) barbitalized dogs were determined by a refined Stewart salt-injection method. From 3–4 determinations were obtained per hour. The constancy of successive measurements is revealed in the following representative results expressed in liters/minute: *23 K. drops*, 2.99, 3.01, 2.65, 2.53, 2.31, 2.39, 2.40; 2.68, 2.88, 3.07, 3.05, 2.66, 3.08; 2.67, 2.75, 2.60, 2.87, 2.66; 2.91, 2.78, 2.80, 2.85, 2.76. *12.5 K. drogs*, 1.51, 1.45, 1.31, 1.27, 1.36; 1.75, 1.97, 1.95, 1.79. These figures yield an estimate of minute outputs in dogs of these weights. On the basis of surface area, 78 per cent of the determinations on all the dogs fell within 2.4–3.4 liters/sq. meter. The mean of 93 measurements on 15 dogs was 2.86 liters/sq. meter (Standard Deviation, 0.51). This compares favorably with observations based on the Fick method reported by Marshall (Am. J. Physiol. **77**: 459, 1926) for unanesthetized dogs.

Calculations of total peripheral resistance based on these output determinations in the large dogs ranged from 2000–6600 A.U. with a mean value of 4185 (σ = 900 A.U.). For the 4 medium dogs, the

variation was 3585–9920 A.U. There was a tendency for TPR to increase progressively after the first two hours of experimentation.

With heart rates that varied from 122–233 beats/min., the stroke volume ranged from 10.8 cc.–22.5 cc. in large dogs and from 7.3–15.2 cc. in medium-sized dogs.

Potassium and the cause of death in traumatic shock. ALEXANDER W. WINKLER and HEBBEL E. HOFF. *Dept. of Internal Medicine and the Laby. of Physiology, Yale School of Medicine.* A form of traumatic shock was produced in twenty-five dogs under dial anesthesia by releasing a tourniquet which had been applied to one hind leg several hours previously. Electrocardiograms and samples of serum for potassium analysis were obtained at intervals until death. The serum potassium regularly increased somewhat above its normal level, and electrocardiograms showed various changes, including at times those usually associated with small increases of the serum potassium. However, the serum potassium did not usually rise above 8 mM per liter, a concentration insufficient to produce any circulatory difficulty in the intact animal, and the electrocardiograms clearly indicated that death did not usually result from potassium poisoning. In two instances only, in dogs living an unusually long time in a state of shock, did the serum potassium concentration rise above 10 mM per liter just prior to death, and in these same two dogs the electrocardiograms indicated that death was due to cardiac arrest from potassium poisoning.

It is concluded that, although in rare instances death in this form of shock may result from autointoxication with potassium, it is due to some other cause in the great majority of cases.

Observations on the polyuria produced by desoxycorticosterone acetate. CHARLES A. WINTER and W. R. INGRAM. *Depts. of Physiology and Anatomy, State Univ. of Iowa.* The dog and the cat differ in their responses to injections of desoxycorticosterone acetate in oil. Dosages up to 30 mgm. daily fail to increase the daily water exchange of normal cats. In cats with experimental diabetes insipidus, similar injections increase neither the severity of the d.i., nor the dosage of pitressin required to relieve it. In the dog, injections of 5 or 10 mgm. daily markedly increase the severity of d.i. already present, or render normal dogs mildly polyuric. Pitressin only partially controls desoxycorticosterone polyuria, even if given in dosage several times that required to render a d.i. animal non-polyuric. During the administration of desoxycorticosterone acetate, reduction of nitrogen intake while the salt intake is kept constant reduces the polyuria, but the change in urine volume is less marked than when a similar experiment is performed on an ordinary d.i. dog. Increase in either salt or nitrogen intake is markedly effective in increasing the polyuria. Creatinine clearances on three d.i. and two normal dogs before and during the injections show no consistent difference between the two groups. In four of the five dogs, the injections decreased the tubular reabsorption of water, as shown by creatinine U/P ratios. The dog that showed no change was a d.i. animal that already had a creatinine U/P ratio as low as 18 before the injections began. In two d.i. and one normal dog, the injections significantly increased the glomerular filtration as shown by the creatinine clearance.

Motor performance of an adult Macaca mulatta following bilateral removal of areas *4* and *6*. CLINTON N. WOOLSEY and PHILIP BARD. *Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* If areas *4* and *6* are removed in stages from both hemispheres of the adult monkey with sufficiently long intervals between operations to permit maximal recovery of function, performance approaching that seen after similar ablations in young monkeys (Kennard, 1942) may be observed.

From a macaque weighing 2.7 kgm. the entire left precentral gyrus was removed in October 1935. The removal extended from the sulcus callosomarginalis to the Sylvian fissure, and from the bottom of the central fissure to the inferior precentral sulcus and the anterior limit of area *4S*. In October 1937 (wt. 4.4 kgm.) the right arm and leg areas were similarly removed, leaving the face area. Although the animal was greatly incapacitated, he was able to sit and to walk on the following day. It was assumed that the motor performances exhibited were made possible by the presence of both areas *6*. In August 1938 both areas *6* were removed together with the right face area. It was anticipated that this would yield a greatly incapacitated animal resembling our decorticate monkey with which we wished to compare it. Surprisingly the operation produced relatively little additional motor difficulty. The animal was able immediately to walk and, when excited, to climb. Subsequently the removals described were confirmed.

Apparently the rate at which recovery proceeds in the adult monkey is much slower than in the infant, and if additional lesions are to be made, sufficient time for maximal recovery of the remaining cortical and subcortical mechanisms must be allowed.

"Second" somatic receiving areas in the cerebral cortex of cat, dog and monkey. CLINTON N. WOOLSEY. *Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* Adrian (1941) described a second somatic receiving area in the anterior ectosylvian gyrus of the cat, responsive to tactile and pressure stimulation of the apices of the contralateral limbs. Since it was not

found in dog or monkey, Adrian suggested the area might serve the specialized claw mechanism of *Felidae*.

Opportunity to study this system arose, during the course in physiology for first-year medical students, in an experiment devoted to the sensory areas of the cerebral cortex. The area was found in 10 cats and in each of 2 dogs examined. Certain views, previously expressed (Woolsey and Walzl, Bull. Johns Hopk. Hosp. 1942, Dec.), led us to deduce that in the monkey the area might be found on the superior wall of the Sylvian fissure. Experiment confirmed the deduction. The area is caudal to the insula, adjacent to the auditory area; its rostral portion receives impulses from the forelimb, its caudal part from the hind.

In both cat and dog the area receives impulses from both sides of the body, chiefly from the apices but also from proximal parts of the limbs. Ipsilateral responses are about half as large as contralateral ones. Responses can be evoked by hair movement alone; in deep anesthesia pressure may be required. In monkey only contralateral responses have been found and only in response to ressure on the digits or over muscles activating gers and toes. It is probably significant that in t the area is directly contiguous to our second auditory area (*loc. cit.*).

A monkey which survived bilateral decortication for 161 days. CLINTON N. WOOLSEY. *Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* Three chronic bilaterally "decorticate" monkeys with survival periods of 26 Karplus and Kreidl, 1914), 33 (McKinley and erkowitz, 1933) and 37 days (Ter Braak, 1936) have been described. The animal here reported lived for more than 5 months with all cortex removed except a bit of neocortex beneath the rostrum and small portions of both hippocampal gyri. No damage was done the thalamus and most of the striatum remained. The decortication was effected in two stages (left, October 1936; right, November 1937).

The early status of this animal was similar to that described by the above authors. Considerable improvement took place, however, and fragments of the righting reactions, progression and other patterned activities appeared. Yawning and several different vocal sounds were possible. Chewing and swallowing movements were present from the beginning but they were not very effective. They increased in vigor and amplitude throughout the survival period. A number of interesting reflexes involving the mimetic and extrinsic ear muscles were evoked from specific reflexogenous zones of the head. These reflexes were not seen in other animals with cortical lesions but were present in one of Dr. Hines' infant monkeys 3 weeks of age. The gastro-intestinal tract was very active and vigorous hunger contractions were recorded. The animal died of an intestinal intussusception.

The functional capacity of the nervous system of this animal appeared limited chiefly by its wasted muscular apparatus. It seems likely that piecemeal decortication would result in a preparation more like decorticate subprimates.

A study of placing and hopping reactions in children. CLINTON N. WOOLSEY and ROBERT A. GOODWIN, JR. (Henry Strong Denison Scholar, 1939–40, during which time this study was made) (by invitation). *Dept. of Physiology, Johns Hopkins Univ., School of Medicine, Baltimore.* Development of placing and hopping reactions in relation to standing and walking was studied in a group of 125 children, aged 4 mos. to 5 yrs., at the Well Baby Clinic of the Eastern Health District of Baltimore. In general, placing reactions (tactile and visual) and hopping reactions appear at the age of 6 months. Both direct and crossed placing reactions occur and exhibit appropriate local signatures. At first all reactions are sluggish but the speed of reaction gradually increases until the child is able to stand alone and walk freely. From a short time after appearance until about the age of 2 the reactions are readily elicited in normal children not actively resisting the examiner. After the age of 2 a feature characteristic of the reaction in monkeys—inhibition—becomes more and more prominent until in children of 4 and older it is difficult to elicit the reactions. Nevertheless, children as old as 5 may respond excellently. Older children, as do monkeys, in hopping lateralward tend to shift from heel to toe instead of lifting the foot free from the floor. A child of 7 with hemiplegia of several months duration gave excellent responses in the normal limbs but failed to react when the spastic hemiplegic members were tested. This investigation carries to man the series of studies on these postural reactions made by Bard and his associates.

Further observations on the effect of feeding a high fat ration on the water, fat and protein content of the skin and body of the albino rat. WINFREY WYNN (by invitation), GLENVILLE GIDDINGS (by invitation) and JOHN HALDI. *Dept. of Physiology, Emory Univ., Ga.* Changes similar to those produced in the composition of the skin of the albino rat by feeding a ration containing a large amount of fat for 70 days (Am. J. Physiol. 135: 392, 1942) can be induced in a much shorter period of time. At the end of one week on the high fat diet the percentage water content of the skin of the males was 57.1 as compared with 61.9 per cent on the stock ration; that of the females on the fat and stock rations 50.1 and 57.4 per cent, respectively. The fat content of the skin was appreciably higher

and the protein content lower on the fat than on the stock ration. Corresponding differences were observed in the water, fat and protein content of the entire body.

The differences in the composition of the skin and body on the stock and carbohydrate rations were not as pronounced as those obtained at the end of 70 days in the previous experiments. The effects produced by feeding the high fat ration two and three weeks were approximately the same as those observed at the end of the first week on the ration.

THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS

Abstracts of papers presented for the annual meeting scheduled for Cleveland, April 6–10, 1943. On account of the cancellation of this meeting, all the papers are to be regarded as "read by title." For possible correction in any of the abstracts see the next issue.

Concentration of higher fatty aldehydes in tissues of vitamin B-deficient rats. MARJORIE ANCHEL and HEINRICH WAELSCH. *Depts. of Neurology and Biochemistry, Columbia Univ., New York.* The members of the vitamin B group are believed to play an important rôle in the synthesis of fat from other body constituents. To test the possible function of the higher fatty aldehydes (h.f.a.) in such conversions, their concentrations in muscle, brain and sciatic nerve of rats on a complete diet were compared, in two sets of experiments, with concentrations in the tissues of rats on a fat-free, vitamin B-deficient diet.

In one experiment, the muscles of the mildly deficient rats had a higher concentration of h.f.a. than those of the normal rats. In a second experiment, determinations carried out in the last two weeks of a severe deficiency showed an increase of the h.f.a. in the nerves but no significant difference in the concentration in brain. In this experiment the concentration in the muscles of the deficient group was below that of the normal animals.

Effect of hemorrhagic anemia on quinine excretion. JAMES C. ANDREWS and W. E. CORNATZER. *Dept. of Biological Chemistry, School of Medicine, Univ. of North Carolina, Chapel Hill.* The purpose of this work was to determine whether any relationship exists between hemorrhagic anemia and the levels of quinine attained in blood and urine after single doses of quinine sulfate. Two male dogs were freed from intestinal parasites. After a period of four days for healing of the intestine, the dogs were given 20 mgm. of quinine sulfate per kilo of body weight by mouth in a gelatin capsule. Blood and urine samples were taken at intervals of 0 and 30 minutes and 1, 2, 4, 6, 12 and 24 hours. Quinine was determined by the method of Kyker, Webb and Andrews.

The curves of blood concentration and urinary excretion of quinine were determined after two such administrations of single doses to the normal animals. Hemorrhagic anemia was then produced by heavy bleeding. After a hematocrit value of 20 per cent was attained for two weeks, quinine administration was repeated. The shape of the blood curves varied from the normal in that under conditions of anemia a higher level of quinine content followed the initial peak. This plateau corresponded somewhat to that found by Andrews and Webb in dogs with moderate hookworm infection and indicates that higher blood levels resulting in some cases from quinine administration to hookworm infected dogs may probably be the results of the anemia which accompanies hookworm infection. No significant change was found in the percentage of recovery of quinine in the urine.

Effect of liver damage on quinine excretion. JAMES C. ANDREWS and W. E. CORNATZER. *Dept. of Biological Chemistry, School of Medicine, Univ. of North Carolina, Chapel Hill.* The demonstration by Anderson of the effect of the liver on the metabolic destruction of ingested quinine, and his preparation from liver of an agent active in this destruction have suggested confirmatory studies from the standpoint of liver damage, accomplished by means of chloroform anesthesia.

Quinine sulfate was administered and blood and urine samples taken and analyzed as described in the preceding abstract. (Andrews and Cornatzer.) After two experimental administrations of quinine to the normal animal the effect of two degrees of chloroform anesthesia was investigated.

In all cases, after chloroform anesthesia the level of quinine in the blood remained up for a markedly longer period than under normal conditions, thus demonstrating decreased metabolic destruction.

The results from urine excretion studies paralleled those from blood. For example, percentage recoveries of the quinine administered to a normal dog were (in two different experiments) 4.4 and 8.9. These recoveries increased to 11.5 per cent after 30 minutes of chloroform anesthesia and to 14.7 per cent after one hour. Four months later

the same animal showed a recovery of 7.5 per cent of the dose. These results confirm the previous conclusions of other workers and ourselves as to the vital rôle of the liver in the metabolic destruction of quinine.

X-ray diffraction of muscles. E. W. Ashkenaz, G. C. Henny and M. Spiegel-Adolf. *Depts. of Colloid Chemistry and Physics, Temple Medical School, Philadelphia.* X-ray diffraction studies were made on living and dried sartorius muscles of Rana pipiens in an attempt to correlate physicochemical changes with differences in the x-ray diffraction patterns.

A special camera was built in which the distances from the object to the focal spot and to the film were 60 and 20 mm. respectively; the necessary exposure time was thus cut down to 6 minutes. Response of the living muscles was tested electrically after each exposure. Living muscles show equatorial orientation at a spacing corresponding to 10.3 Å and indications of a flattening of the outside ring. Drying at room temperature in vacuo intensifies this picture, the spacing of the sickle corresponding to the spacing of 5.4 Å reported by Astbury. Stretching of the muscle close to the breaking point brings forth an additional spacing in the dried muscle pattern which can be identified with a similar diffraction line given by stretched tendon. X-ray irradiation up to 23,400 r does not modify the diffraction pattern of subsequently dried muscle. Equatorial orientation is lost upon faradic stimulation but not upon exposure to effective caffeine concentrations, provided that shortening of the muscle is mechanically prevented. The x-ray diffraction patterns of cut muscles temporarily immersed in isotonic $CaCl_2$ or hypertonic NaCNS or NH_4Cl solutions show no orientation, corresponding to a loss of birefringence. Changes produced by $CaCl_2$ are reversible; $MgCl_2$ does not give similar effects. NaCNS and CH_3COOH cause changes in the spacings of the x-ray diffraction patterns suggesting changes in hydration. [*Kathryn McHale Fellow.*]

Activation of soybean lipoxidase. Bernard Axelrod and Marian W. Kies. *Enzyme Research Laby., Bur. Agricultural Chemistry and Engineering, Agricultural Research Administration, U. S. Dept. of Agriculture, Washington.* A considerable purification of soybean lipoxidase has been effected by a procedure involving ammonium sulfate precipitation, pH control, dialysis, and precipitation of other proteins by purothionin. With purified lipoxidase, it was possible to demonstrate the existence of a substance in soybean meal which accelerates the enzymatic oxidation of linoleic and linolenic acids and the concurrent oxidation of co-substrates such as ascorbic acid, carotene, certain leuco dyes, pyrogallol, etc.

In a typical experiment nine times as much linoleic acid was oxidized in three minutes by enzyme with activator as by enzyme alone.

A crude preparation of activator may be obtained by extracting defatted soybean meal with dilute acetic acid at 95° C. The activator in the filtrate may be concentrated by $HgCl_2$-H_2S treatment. Further purification is achieved by fractional precipitation with alcohol.

The amount of activator necessary for optimum oxidation of the unsaturated fat depends on the concentration of fat in the substrate mixture. Increasing the concentration of fat increases the need for activator. This may explain the inhibition of soybean lipoxidase by high fat concentrations reported by Sumner and Sumner (J. Biol. Chem., **134**: 531, 1940).

The "purified" activator material is largely polypeptide in nature, and loses its activity on digestion with papain. [*Work done on Bankhead-Jones Funds, SRF-2-9.*]

Effect of injection of individual amino acids upon the Emge sarcoma in rats. Howard H. Beard. *Dept. of Biochemistry, School of Medicine, Louisiana State Univ., New Orleans.* Most of the amino acids of the protein molecule, except tyrosine, were injected individually daily for 3 weeks into young rats bearing the Emge sarcoma (3 cc. of physiological saline containing 18 mgm. of a given amino acid). Injections were begun the day of transplants. The average increase in tumor growth in 291 control tumor rats was 28 grams as compared to 9 grams in 368 "amino acid" rats. In the controls 7 out of 280 tumors disappeared spontaneously. In all, 164 out of 348 tumors, or 47 per cent disappeared under amino acid injections. These results confirm those obtained in our last study in which 83 per cent (38 out of 46) in one group and 60 per cent (15 out of 26) of the tumors disappeared after amino acid injections beginning the day of transplants.

The per cent disappearance of tumors was as follows: arginine + histidine, 100; arginine, 70, 93; lysine, 83; arginine + lysine, 79; phenylalanine, 75; valine, 74; tryptophane, 64; alanine, 63; methionine, 59; histidine, 56; leucine, 50; norleucine, 44; isoleucine and cystine, 43; serine, 40; aspartic acid, 38; proline, 25; glutamic acid, 22; glycine, 18; cysteine, 17; hydroxyproline, 13; threonine, 13. It is interesting to note, with one or two exceptions, that the essential amino acids occupy the first 10 positions in regard to the disappearance of tumors.

Effect of injection of individual amino acids and a casein hydrolysate upon Emge sarcoma in rats. Howard H. Beard. *Dept. of Biochemistry, School of Medicine, Louisiana State Univ., New Orleans.* Eighteen milligrams of a given amino acid were injected daily in 3 cc. of physiological saline beginning the *day of transplantation*

or 2 weeks later. The casein hydrolysate (10 per cent Amigen) was injected in 2 cc. amounts daily or 30 cc. daily in place of the drinking water. Injection of the amino acids (arginine + histidine, phenylalanine, alanine, valine, leucine, glutamic acid and proline) or feeding cystine by mouth, caused 39 out of 53 tumors, or 74 per cent to disappear as compared to 1 in the controls. When the amino acids were injected 2 weeks *after* transplantation of the tumors, only 20 out of 170 tumors, or 9 per cent disappeared, compared to none in the controls. To our surprise the injection or ingestion of the casein hydrolysate had no effect upon the tumor characteristics as compared to their controls. This is in contrast to the results of others who have shown that a neutralized muscle hydrolysate will cause tumors to disappear. Evidently something more than the amino acids is necessary, e.g., the nitrogenous bases of the muscle tissue (Roffo, A. H. Bol. Institut. de Med. Exper. para el estud. y trat del Cancer, 14: no. 45, 257, 1937. Boyland, E. Biochem. J. 35: 1283, 1941. Lustig, B. and H. Wachtel, Ztschr. Krebsforsch. 43: 54, 1935. We are studying this question at the present time.

The reaction of chorionic gonadotropin with phenylisocyanate. FRITZ BISCHOFF. *Chemical Laby., Santa Barbara Cottage Hospital Research Inst., Santa Barbara, Calif.* More than 90 per cent of the physiologic activity of chorionic gonadotropin is destroyed by phenylisocyanate under the specific mild conditions of reaction which inactivate the mare serum gonadotropin and which were formerly regarded as confined to reaction with the amino group.

Influence of vitamin B_6 and pantothenic acid upon the growth of sarcoma 180. FRITZ BISCHOFF, LOUISE P. INGRAHAM and J. JEROME RUPP. *Santa Barbara Cottage Hospital, Santa Barbara, Calif.* In three series of experiments using 122 Marsh-Buffalo mice, the maintenance on a synthetic diet containing vitamins of the B group other than B_6 produced a marked and significant decrease in tumor rate growth, which was corrected by the addition of vitamin B_6 without significantly changing caloric intake. In two series of experiments running concurrently with the vitamin B_6 experiments (31 additional mice), pantothenic acid deficiency was without influence upon rate of tumor growth. In a single experiment comprising 30 mice, the addition of vitamin B_6 to a diet otherwise completely deficient in the B complex, produced a significant increase in tumor growth. With the exception of a decrease in thymus weight, no characteristic pathology was observed in the mice deficient in vitamin B_6.

Investigation of the α and β phospholipid fractions. CHESTER F. BURMASTER. *Dept. of Biochemistry and Pharmacology, Univ. of Rochester Medical School, Rochester, N. Y.* Micromethods have been developed, using variations of the Malaprade reaction, for the analysis of serine, ethanolamine, α-glycerophosphate and β-glycerophosphate in the aqueous extract from the alkaline hydrolysis of phospholipids.

By use of these methods on pure samples of α- and β-glycerophosphates, as well as their mixtures with serine, ethanolamine, inositol and choline, both before and after treatment with alkali for periods of time found sufficient to hydrolyze phospholipid completely, no shift from the β-form to the α-form or the reverse was found. This finding does not agree with conclusions recently reached by Folch (J. Biol. Chem. 146: 31, 1942) concerning the stability of α-glycerophosphate in alkaline hydrolysis of phospholipids.

These methods were then applied to the analysis of the α-and β-cephalins and α- and β-lecithins prepared from egg yolk according to the procedures developed by Yokoyama and Nishimoto (Proc. Imp. Acad. Tokyo 9: 582, 1934; Nishimoto, U., ibid. 10: 578, 1934). Their "α-cephalin" fraction averaged 49 per cent α and 52 per cent β; the "β-cephalin" fraction averaged 47 per cent α and 53 per cent β compared with 49 per cent α and 51 per cent β for the whole cephalin fraction. The "α-lecithin" fraction averaged 55 per cent α and 45 per cent β and the "β-lecithin" fraction 46 per cent α and 54 per cent β. The idenitty of these fractions is being investigated.

The procedure is also being applied to the individual cephalin fractions prepared by the method of Folch, J. Biol. Chem. 146: 35, 1942.

The B vitamins and protein metabolism in the rat. M. L. CORNETT and E. W. MCHENRY. *School of Hygiene, Univ. of Toronto.* Previous investigations from this laboratory have indicated that both thiamin and pyridoxine must be supplied to enable fat to be synthesized from protein. In the present work rats were depleted of thiamin and pyridoxine on a casein diet, free of carbohydrate and fat. Using isocaloric feeding in a subsequent supplemental period, the effects of thiamin and pyridoxine on glycogen synthesis were studied. Neither vitamin alone had any effect but when given together there were significant increases in both liver fat and liver glycogen. It is concluded that both thiamin and pyridoxine are necessary for the formation of glycogen from protein.

Effect of intravenous casein hydrolysate on the amino nitrogen and CO_2 combining power of plasma. WARREN M. COX, JR. and ARTHUR J. MUELLER. *Mead Johnson Laboratories, Evansville, Ind.* Because the rapid injection of amino acid mixtures or protein hydrolysates has occasionally resulted in nausea, observations have been made on the amino nitrogen level and CO_2 com-

bining power of the blood plasma of dogs during and subsequent to a rapid intravenous injection of an enzymic casein hydrolysate. The rate of injection was constant, 0.27 cc. of a 10 per cent solution per minute per kilo body weight for 120 minutes, and solutions of pH 4.5, 5.5., 6.5 or 7.5 were used. Blood samples were taken at half-hour intervals during injection, and for 3½ hours afterwards. The same dogs were used repeatedly for 15 periods.

Vomiting did not occur after the second injection in the same dog. Plasma NH_2-N rose an average of 17.4 (σ 2.7) mgs. per 100 cc. during the injection, and fall 11.2 (σ 1.9) mgs. in the first 30 minutes after cessation. It returned promptly to the normal level. Neither the amount of rise nor the fall bore any relation to the pH of the solution. Fall in CO_2 combining power was definitely related to the pH of the solution. The fall in volume per cent as read at the end of the 2 hour injection was, at pH 4.5, 19.0; pH 5.5, 14.2; pH 6.5, 12.2, and pH 7.5, 5.5.

Neither of these values provides an adequate explanation for nausea from rapid injection of protein hydrolysates.

A quantitative method for the determination of tyrothricin. KEENE DIMICK. *Western Regional Research Laby., Bureau Agricultural Chemistry and Engineering Agricultural Research Administration, U. S. Dept. of Agriculture, Albany, Calif.* The well known hemolytic property of tyrothricin (gramicidin plus tyrocidine) has been made the basis of a quantitative method for the determination of this bactericide in bacterial cultures. The degree of hemolysis of standard suspensions of rat erythrocytes is measured by light transmission methods with a Klett-Summerson photoelectric colorimeter. The degree of hemolysis was found to be proportional to the amount of tyrothricin added to the erythrocyte suspension. From these results a straight-line calibration curve, covering the range of 4 to 10 μg., was constructed. The amount of hemolysis produced by an unknown solution was measured with the colorimeter and the tyrothricin content was read directly from the calibration curve.

For the assay of culture media, a known volume of the culture is added to 9 times its volume of 95 per cent alcohol, shaken, and centrifuged. The clear supernatant fluid is tested by adding 0.5 ml. to the standard suspension of erythrocytes. Only 0.1 ml. of a bacterial culture containing approximately 100 μg. of tyrothricin per ml. is necessary to determine the concentration with an accuracy of ±5 per cent. The accuracy of the method was determined by adding known amounts of tyrothricin to a culture medium and comparing the analytical results with the known concentrations of bactericide.

Maintenance of adrenalectomized rats with urinary extracts. RALPH I. DORFMAN and BENJAMIN N. HORWITT. *Brush Foundation, Dept. of Biochemistry, Western Reserve Univ.; Dept. of Medicine, Lakeside Hospital, Cleveland.* Previously we reported the presence of cortin-like material in extracts of men's urine by means of a technique involving the relative lack of resistance of adrenalectomized rats to cold. We now have been able to demonstrate that these extracts can also maintain the life of adrenalectomized rats.

Young, adrenalectomized male rats were placed on a diet of Purina dog chow. From the third to the ninth day inclusive, the rats received daily by stomach tube the preparations in 1 cc. of 10 per cent ethanol. Group A (9 animals) received only the 10 per cent ethanol; group B (8 animals) received the equivalent of 0.2 cc. of adrenal cortical extract; group C (9 animals) received the equivalent of 0.1 cc. of adrenal cortical extract; group D (9 animals) received the extract equivalent of 1 liter of men's urine. The urinary material was an *alkali insoluble* fraction of an ethylene dichloride extract of men's urine.

All the rats in groups B, C and D were alive when treatment was stopped. At this time, 7 of the 9 rats in group A were dead. The remaining 2 animals died two days later. Between the second and tenth day after treatment of groups B, C and D was stopped, all the animals died. The average survivals in days of the various groups were 7.4, 16.7, 16.0 and 16.8 for groups A, B, C and D, respectively. [*Supported in part by a grant from the Josiah Macy, Jr. Foundation.*]

State of nucleic acid in isolated nuclei. ALEXANDER L. DOUNCE. *Dept. of Biochemistry, Univ. of Rochester Medical School, Rochester, N. Y.* Nuclei have been isolated from rat liver at pH 6.0–6.2, and at pH 3.8–4.0. From Walker carcino-sarcoma 256, nuclei have been isolated at pH 3.8 or slightly lower. Chicken erythrocyte nuclei have been prepared by an improved method at pH 6.8–7.0.

It has been found that the nucleic acid of the isolated nuclei may exist largely in an easily extractable state, or that under different conditions much of it may be firmly bound and unextractable by the usual mild methods. Liver or tumor nuclei prepared at the low pH values, as well as erythrocyte nuclei prepared at pH 6.8–7.0, contain the firmly bound nucleic acid. These nuclei will form a curious semi-transparent gel which persists in high dilution, if the pH is raised to 8.5 with ammonia in the absence of other electrolytes. The erythrocyte nuclei also form a gel in five or ten per cent sodium chloride solution.

On the other hand, liver cell nuclei prepared at pH 6.0 will not form such a gel, and the nucleic acid is almost entirely extractable, together with

protein, in five per cent sodium chloride solution. Desoxyribonucleic acid extracted from whole tissue by mild methods must also be loosely combined.

The fact that chicken erythrocyte nuclei contain the firmly bound nucleic acid argues in favor of the hypothesis that the firmly bound state of desoxyribonucleic acid is of physiological importance and is not merely an artifact caused by low pH.

A spectrophotometric study of the reaction of protohemin with various proteins and with peptone. DAVID L. DRABKIN. *Dept. of Physiological Chemistry, School of Medicine, Univ. of Pennsylvania, Philadelphia.* In 0.1 M NaOH hemoglobin is rapidly denatured and converted into globin hemochromogen. This reaction suggests that the affinity of denatured globin for protohemin is great, since only 1 mole of hemin is available per equivalent weight (17,000) of globin. Actually, it has been found that more hemin can combine with globin than 1 mole per 17,000 equivalent weight unit. A quantitative study has been made of the reaction of protohemin with various proteins.

Upon the addition of protohemin to hemoglobin or globin in 0.1 M NaOH with $Na_2S_2O_4$, the amount of reduced globin hemochromogen increased linearly per mole of hemin added until approximately 4 moles of hemin had combined per 17,000 equivalent weight of globin. The reaction then tapered off. Analysis of the spectrophotometric data suggests that a total of 32 moles of hemin can coordinate with a 68,000 molecular weight unit of globin.

Similar results have been obtained in the reaction of protohemin with cytochrome *c*, egg albumin, and edestin in solutions of pH 10 to 13. Undenatured hemoglobin, cytochrome *c*, and egg albumin at pH 7 to 9, as well as peptone (Difco) at pH 13, failed to react with hemin. Partial hydrolysis of egg albumin with acid resulted in a marked reduction in the affinity (of the products) at pH 13 for hemin.

It is suggested that groups capable of actively reacting with hemin are exposed upon alkaline denaturation of the proteins studied. The formation of the protein hemochromogens cannot be correlated with the content of histidine in the proteins.

The water and electrolyte content of brain. LILLIAN EICHELBERGER and RICHARD B. RICHTER. *Dept. of Medicine, Univ. of Chicago.* Total water, nitrogen and the concentration of the principle electrolytes were determined on brain, which was removed by bilateral craniotomy from normal dogs. For analyses the brain was separated into 1) right hemisphere, 2) left hemisphere, and 3) cerebellum with the brain stem.

The right and left hemispheres from the same animal gave the same analytical results. The hemispheres gave the following mean average results which are expressed as units per kilo of hemisphere: total water, 764 gm., $\sigma \pm 7.5$; chloride, 36.8 mM, $\sigma \pm 1.3$; sodium, 50.4 mM, $\sigma \pm 1.7$; potassium, 96.5 mM, $\sigma \pm 3.5$; calcium, 1.02 mM, $\sigma \pm 0.07$; magnesium, 5.98 mM, $\sigma \pm 0.48$ and total nitrogen 19.1 gm., $\sigma \pm 0.5$.

The cerebellum with brain stem gave the following mean average results: total water, 747 gm., $\sigma \pm 8.8$; chloride 35.1 mM, $\sigma \pm 0.9$; sodium, 50.8 mM, $\sigma \pm 1.98$; potassium, 94.4 mM, $\sigma \pm 1.5$; ans total nitrogen, 19.2 gm., $\sigma \pm 0.6$.

Because the analyses of the hemispheres and the cerebellum following extraction of the dried tissues with ether and petrolic ether gave low concentrations of chloride, sodium, potassium and magnesium, the analytical results were not expressed in terms of fat-free tissue.

Distribution of sulfocyanate, radioactive chloride and sodium in the dog. J. R. ELKINTON, A. W. WINKLER and A. J. EISENMAN. *Yale Univ. School of Medicine.* Under a wide range of circumstances the apparent volume of distribution of sulfocyanate in the dog regularly exceeds that of Cl^{38} and of Na^{24}. Taking the volume of distribution of Cl^{38} as unity, in 38 trials the average volume of distribution of Na^{24} was 1.25 and that of sulfocyanate 1.52. It is concluded that sulfocyanate in the dog is distributed through a volume considerably in excess of the extracellular fluid. Changes in the volume of distribution of all these substances with hydration and with rehydration were usually closely proportional, in spite of these differences in absolute magnitude. Sulfocyanate distribution may therefore be used as a relative but not as an absolute measure of extracellular fluid.

Oxygen uptake caused by an iron-protein with ascorbic acid, phospholipid and amino-acid. K. A. C. ELLIOTT and B. LIBET. *Inst. of the Pennsylvania Hospital, Philadelphia.* It was previously reported (Federation Proceedings 1: 122, 1942) that a thermostable material obtained from liver causes a marked temporary stimulation of the respiration of brain and liver suspensions. This material is a reddish-brown protein containing iron. Its effect is greatly increased by low concentrations of neutralized ascorbic acid but slowed by higher concentrations.

Purified phospholipid from brain, with low concentrations of ascorbate and the iron-protein, take up oxygen very rapidly. Without ascorbate, oxygen uptake is negligible; without iron-protein, it is very slow. With liver phospholipid and ascorbate alone the rate is considerable, but is increased by the iron-protein. Cerebrosides are inactive. Ascorbate and iron-protein alone take up no oxygen. (Both phospholipid and the iron-

protein inhibit copper catalysis of ascorbic acid oxidation.) Ascorbate cannot be replaced by glutathione or cysteine.

With tissue suspensions, the effect of iron-protein plus ascorbate is considerably increased by the addition of various *d* or *l* amino-acids, especially phenylalanine. This effect depends upon additional factors since phenylalanine has little effect with purified phospholipid plus ascorbate plus ron-protein. Dihydroxyphenylalanine and phenylpyruvic acid inhibit the system.

No extra CO_2 is produced by the system with tissue suspension or phospholipid.

A ferritin preparation from horse spleen was much less active than our iron-protein. With inorganic iron as catalyst, the oxygen uptake curves obtained with phospholipids or tissue suspensions, and the effects of ascorbic acid, vary with the buffer used and usually differ from the results with the iron-protein.

Liver cirrhosis and choline. R. W. ENGEL. *Laby. of Animal Nutrition, Alabama Polytechnic Inst., Auburn.* Hepatic cirrhosis was produced consistently in 9 weanling rats fed a choline-deficient diet containing 20 per cent protein and 6 per cent fat. The diet consisted of alcohol-extracted casein 6, alcohol-extracted peanut meal 30, sucrose 54, salts 4, and lard 6 per cent; and was supplemented with adequate amounts of carotene, calciferol, α-tocopherol, thiamin, riboflavin, pyridoxin, calcium pantothenate, inositol, and p-aminobenzoic acid.

To prevent the fatal choline-deficiency renal hemorrhage during the rapid growth period, 4 of the rats received 20 mgm. of choline chloride each daily for 6 weeks; the others received small amounts of choline during the first 4 weeks of the experiment only when palpably enlarged kidneys indicated hemorrhage. The former group gained well and reached normal mature body weight; the latter group made irregular gains and remained stunted. The animals were on experiment for 16 months.

Gross appearance at necropsy indicated varying degrees of hepatic fatty infiltration and cirrhosis. In mild cases the livers were enlarged, fatty, and had only a slightly roughened surface, but in the severe cases they were dark, shrunken, and had the typical nodular "hobnail" surface of advanced cirrhosis. Microscopically, the lesions varied from mild periportal fibrous tissue proliferation to extensive proliferation so that the liver parenchyma was divided into sharply circumscribed lobules of varying size and shape.

That choline deficiency was responsible for the cirrhosis was adequately demonstrated. It was entirely prevented in 10 rats receiving the same diet plus 20 mgm. of choline chloride each daily throughout the experiment.

Certain features of salt catalysis. MARK R. EVERETT, FAY SHEPPARD and LOUIS E. DIAMOND. *Dept. of Biochemistry, Univ. of Oklahoma School of Medicine, Oklahoma City.* Hydrogen peroxide oxidation of carbohydrates in aqueous solutions containing iron salt, copper salt, alkali bicarbonate or tungstate, causes rapid formation of aldoses, ketoses, and alduronic, keturonic and dicarboxylic acids at room temperature. With iron salts, sufficient peroxide is utilized to remove 2 to 5 hydrogen atoms from various hexose derivatives. The oxidation apparently involves coordination of hydroxyl radicals with ferric, cupric, bicarbonate or tungstate ions. The oxidation products, and presumably the coordination positions, differ for the several salts. Catalytic activities of the ions do not parallel their ability to decompose hydrogen peroxide. Theoretically, the active ions could react with hydrogen peroxide to form percompounds and unstable ternary complexes.

Ferrous and ferric salts are equally effective catalysts; addition of *d*-gluconolactone does not change their primary valence. In the presence of hydrogen peroxide, ferricyanide reagent does not differentiate ferrous from ferric ions. Unlike the result in ferrous salt solutions, oxidation of ferrous to ferric ions is not quantitative in the ferrous ternary mixture. The ferric iron formed is reduced slowly by accumulating carbohydrate oxidation products. Soluble ferric salts give Trillat's "peroxide" test more intensely after addition of hydrogen peroxide. Since ferrous ions prevent this effect, Trillat's test is positive for only a few minutes with the ternary mixture made from ferric salt. Iron salts exhibit maximal catalysis at much lower molar concentrations than do cupric salts, bicarbonates or tungstates, whose ternary mixtures do not give Trillat's test. Cupric ternary mixtures give positive benzidine "peroxide" tests; they contain no detectable cuprous ion.

The formation of cysteine from methionine in the presence of liver slices. NORMAN F. FLOYD and GRACE MEDES. *Lankenau Hospital Research Inst., Philadelphia.* It has been demonstrated that methionine, incubated under aerobic conditions with liver slices, gives rise to two products which can be determined quantitatively, (1) sulfate, which amounts to 2 per cent of the added methionine and (2) deaminated methionine, α-keto-γ-methiobutyric acid, which varies from 20 to 30 per cent.

Disappearance of added methionine was followed by three methods, (a) the Lavine methionine determination, which does not occur if the amino group is absent; (b) the peroxide oxidation of the sulfur to the sulfoxide, and (c) the McCarthy-Sullivan colorimetric procedure.

With liver slices, it was found that methionine disappeared to the extent of twenty per cent; the

Lavine determination, however, always indicated a slightly greater loss of methionine than the peroxide oxidation or the Sullivan determination. When brei was substituted for slices, the Lavine determination showed that about forty per cent of the added methionine disappeared but the peroxide oxidation revealed little or no change in the sulfur atom. With benzoyl methionine as substrate, the Lavine determination was not applicable, but the peroxide oxidation indicated a loss of methionine with slices, but not with brei.

By inhibiting the oxidation of cysteine formed from added methionine, with sodium pertitanate, yields of cysteine representing 1 to 2 per cent of the methionine were obtained. Homocystine alone was inactive under these conditions, but when choline was present cysteine was produced in the order of 0.2 to 0.3 per cent of the added substrate.

Comparison of the lipotropic effects of choline, inositol and lipocaic in rats. GERTRUDE GAVIN, JEAN M. PATTERSON and E. W. MCHENRY. *School of Hygiene, Univ. of Toronto.* A comparison of the lipotropic effects of choline, inositol and lipocaic has been made with various types of dietary fatty livers in rats. Choline is effective for thiamin fatty livers, partially effective with cholesterol fatty livers, but shows little activity with biotin fatty livers. Against this last type both inositol and lipocaic are active. Lipocaic differs from inositol in being ineffective against fatty livers caused by feeding cholesterol with a high-fat diet. Inositol shows no activity with thiamin fatty livers; the addition of other B vitamins permits inositol to be lipotropic.

Nitrogen distribution in the coagulable liver proteins of normal and selenized rats. ROSS A. GORTNER, JR. *Dept. of Biology and Chemistry, Wesleyan Univ., Middletown, Conn.* Protein preparations from a series of livers from three normal rats and six rats which were maintained for 6 to 8 weeks on high protein diets containing 35 parts per million of sodium selenite have been subjected to micro Van Slyke analysis. No significant differences in the various nitrogen fractions were observed between the control livers and those which exhibited grossly only slight or no apparent selenium pathology. The basic phosphotungstate precipitates from two livers showing severe selenium damage differed from those of other liver preparations by having appreciably higher contents of amino nitrogen; analyses for the individual amino acid components suggested that this resulted from an increased lysine content, since the values for arginine, histidine, and cystine fell within the normal range.

In all preparations excepting those from livers showing severe pathological changes the amino acid constituents of the basic phosphotungstate precipitates accounted for only 90 to 95 per cent of the total nitrogen of these fractions. The balance was considered to be purine nitrogen derived from nucleoprotein. This assumption was corroborated by the analysis of casein to which guanine hydrochloride was added. The phosphotungstate fraction of the preparations from the severely pathological livers contained smaller amounts of purine nitrogen, possibly indicative of nuclear degeneration in this organ. Histological sections of these livers showed destruction of the nuclear reticulum and clumping of the chromatin material.

Canine cystinuria. Urinary excretion of cystine following the administration of homocystine, homocysteine, and some derivatives of cystine and cysteine. W. C. HESS and M. X. SULLIVAN. *Georgetown Univ., Washington.* In previous publications we have studied the excretion of urinary cystine in two male, cystinuric Irish terriers following the ingestion of various levels of casein and arachin, alone or supplemented by methionine, cystine or cysteine. Since the excretion of cystine could be increased by feeding either methionine or cysteine it seemed desirable to study further the effect of feeding —SH compounds especially derivatives of cysteine, upon the excretion of urinary cystine.

The following compounds were prepared and fed; homocystine, homocysteine, diglycylcystine, glycylcysteine, thiazolidine carboxylic acid, S-methyl carboxycysteine, tetrapotassium tetracarboxymethylcystine diacetate, and dipotassium dicarboxy methylcysteine acetate. Of all the compounds fed only two produced any extra urinary cystine, homocysteine, and glycylcysteine and these in small amounts as compared with feeding cysteine. The three other derivatives of cysteine in which either the sulfur or the amino goup or both were substituted failed to influence urinary cystine excretion.

Phosphorus turnover of blood and liver lipids of the fasting mouse. HAROLD CARPENTER HODGE, P. L. MACLACHLAN, W. R. BLOOR, EILEEN A. WELCH and SYLVIA LEVY. *Dept. of Biochemistry and Pharmacology, Univ. of Rochester.* Young, adult, male, albino mice were fasted in groups of 15 for periods through 5 days. Twenty-four hours prior to sacrifice radioactive phosphorus was administered as disodium acid phosphate solution intraperitoneally.

A lipemia was observed which subsided after the third day of fasting, and in which the blood phospholipids were sharply elevated. The turnover of blood phospholipids, as is shown by P^{32}, went through a pronounced maximum with its peak on the second and third days of fasting.

The liver phospholipids were fractioned into α and β forms. The α lecithin and β cephalin tended to disappear from the livers during fasting.

β lecithin and α cephalin tended to remain constant in amount during fasting. The turnover in P^{32} in α and β lecithin, and in β cephalin followed, roughly, a single pattern of sharp increase reaching a maximum on the second fasting day and thereafter decreasing. In contrast, in α cephalin, the P^{32} turnover varied only slightly from day to day.

The production of hypercalcemia with small amounts of vitamin D. JAMES H. JONES. *Dept. of Physiological Chemistry, School of Medicine, Univ. of Pennsylvania, Philadelphia.* The inclusion of one I. U. of vitamin D per gram in a diet very low in phosphorus and high in calcium produced a definite hypercalcemia in rats. Various forms of vitamin D, such as irradiated ergosterol, pure calciferol, or irradiated 7-dehydrocholesterol were equally effective. Dihydrotachysterol (A.T. 10) was much less effective.

The degree of hypercalcemia produced was, in general, proportional to the amount of calcium in the diet. Diets were fed containing approximately 0.03, 0.3, 0.5 and 1.0 per cent calcium. On the lowest level of calcium no hypercalcemia was produced, but the tendency to a hypocalcemia was lessened by the vitamin D. On the intermediate levels of calcium in the diet the serum calcium was usually increased from 1 to 3 mgm. per cent, and on the highest intake of calcium the increase was usually greater than 3 mg. per cent, reaching levels above 15 mgm. per 100 ml. of serum.

Although there was considerable variation, growth was definitely lessened if the serum calcium exceeded 15 mgm. per 100 ml. When no hypercalcemia was produced or when it was of only moderate degree growth of the animals receiving the vitamin was about the same as that of the animals on the same diet but without the vitamin supplement. In all cases the vitamin prevented the development of rickets as judged by examination of the wrist bones according to the "line test technique," and calcification was increased as shown by the percentages of femur-ash.

Influence of processing on thiamin, riboflavin and nicotinic acid content of rice. M. C. KIK and F. B. VAN LANDINGHAM. *Univ. of Arkansas, College of Agriculture, Fayetteville.* Preliminary experiments showed that when rough rice had been exposed to vacuum treatment followed by hydraulic pressure and steam treatment, the water soluble vitamins of the outer layers penetrate the grains during the treatment. Considerable more of these vitamins thus have been retained in rough rice after it has been milled. In this rice conversion method (H. R. Rice Conversion. Rice Conversion, LTD, London 1940) up to 63.5 per cent more thiamine, up to 34 per cent more riboflavin and up to 61.2 per cent more nicotinic acid were retained after conversion than before conversion. This method is also more economical since there is less breakage during milling. [*Aided by a grant from the Williams-Waterman Fund of Research Corporation.*]

The effect of insulin on amino acid metabolism. ALFRED E. KOEHLER, ELLEN BUTTENWIESER and ELSIE HILL. *Sansum Clinic and Santa Barbara Cottage Hospital, Santa Barbara, Calif.* A group of 12 fasting subjects with uncontrolled diabetes mellitus were each given 30 grams of glycine or alanine by means of constant rate intravenous injection over a 2 hour period. The blood and urine amino acid, urea and nonprotein nitrogen were determined at the end of injection and at intervals thereafter. Later, while the subjects were on the same diet, but with the diabetes completely controlled with insulin, the injections were again repeated in a similar manner. Insulin had no significant effects on the blood amino acid, urea or nonprotein nitrogen curves or on the urinary excretion of these substances. The extra urea in blood and urine presumably formed from the injected amino acids was approximately the same in the treated as in the untreated group. There were no appreciable differences between the responses to glycine or alanine.

Our experiments are interpreted as indicating that insulin does not directly influence amino acid metabolism in diabetes mellitus.

The effect of intravenous administration of vitamin A. ALFRED E. KOEHLER and ELSIE HILL. *Sansum Clinic and Santa Barbara Cottage Hospital, Santa Barbara, Calif.* A highly dispersed colloidal solution of vitamin A can be prepared by dissolving the pure crystalline vitamin in a small quantity of propylene glycol and then pouring the solution into water, normal saline, or isotonic glucose solution. Such a colloidal solution containing as much as 100 mgm. (300,000 I.U.) can be given intravenously at constant rate over a 2 hour period without any apparent untoward effects to human subjects. Injections were given to 14 subjects, some with a low vitamin A intake and others with a normal or above normal intake. Several subjects had as many as 4 injections over weekly intervals.

The changes in blood serum concentration of vitamin A were followed by spectrophotometric absorption studies for 48 hours. In general the injected vitamin A was removed so rapidly from the blood stream that little or no increase of the vitamin could be detected regardless of the previous level of vitamin A intake or the initial blood serum level.

Repeated injections, or prolonged oral administration of vitamin A may raise the fasting level of vitamin A in the serum but only up to certain levels, usually less than 100 gammas per 100 cc.

Spectrophotometric studies of the blood serum lipids, saponified in an atmosphere of nitrogen, gave no indications that after the intravenous

injection of vitamin A any alteration in the ultra violet absorption spectrum occurred due to the formation of new compounds.

Quinine administration during progressive vitamin B complex deficiency. GRANVIL C. KYKER. *Dept. of Biological Chemistry, School of Medicine, Univ. of North Carolina, Chapel Hill.* Definite knowledge explaining the metabolism of quinine is lacking. Such information is highly significant in advancing studies on antimalarials and malaria. This study intended the testing of a possible course of metabolic degradation of quinine involving preliminary interaction with certain members of the vitamin B complex, which members and reactions bear analogy in certain established metabolic processes.

To twelve rats of weaning age doses o 20 mgm. of quinine per kgm. of body weight were administered daily throughout the experimental period. During the first experimental period the diet was free from vitamin B complex. To this, yeast and liver were added liberally after severe deficiency symptoms appeared. All urine from each cage was collected daily, pooled and analyzed twice weekly for quinine. Thus average daily excretions were followed during the progress of developing deficiency symptoms, the recovery from the same, and to maturity.

The percentage of the dose which was excreted decreased with progression of the deficiency, remained low for three to five days after liver and yeast supplement, then rose rapidly for about two weeks and was more irregular after considerable growth was accomplished.

In another series, total excreta were collected together in which the total quinine output remained about the same throughout.

This suggests a relationship between absorption of quinine and vitamin intake. Work to establish fecal and urinary excretion and the member of the B complex bearing on the absorption and metabolism of quinine is being continued.

Photodecomposition of quinine. GRANVIL C. KYKER and W. E. CORNATZER. *Dept. of Biological Chemistry, School of Medicine, Univ. of North Carolina, Chapel Hill.* Reference to the instability of quinine standard solutions when exposed to light has been mentioned by several investigators. Preliminary confirmation of this was made previously by one of us (G. C. K.). This study was designed to reveal something of the nature of the photodecomposition.

Nine series of 0.5 per cent quinine hydrochloride solutions were prepared, each differing only in their solvents, as follows: (1) 50 per cent alcohol made slightly alkaline, (2) water, (3) 0.03 N HCl, (4) 0.06 N HCl, (5) 0.125 N HCl, (6) 0.25 N HCl, (7) 0.5 N HCl, (8) 1.0 N HCl, and (9) 2.0 N HCl. Each series contained several identical members. One member from each series was removed simultaneously from exposure to direct sunlight. Variable exposures of each of six members of each series were: 5, 10, 20 hours, 1 week, 1 month, and 3 months. The quinine content of each was expressed by (a) direct silicotungstate formation and estimation, (b) ether extraction and silicotungstate estimation, and (c) optical rotation.

Stability as judged by each of the methods varied but optimum stability was observed by all methods in series (4). This optimum was not sharp and gradiently decreased in either direction. Fifty per cent decomposition occurred in one week in series (1) and (9) and after three months in series (4).

Continuance of the study through extended exposures, with the tracing of the decomposition from the beginning with a photofluorometer, is in progress.

Quinine analytical interference studies. GRANVIL C. KYKER and DOROTHY PLONK. *Dept. of Biological Chemistry, School of Medicine, Univ. of North Carolina, Chapel Hill.* The study of the response of cinchonas to the photelometric estimation of quinine reported previously (Fed. Proc. 1: no. 1, 120, 1942) was extended to cover other cinchonas and derivatives, various non-cinchona alkaloids, synthetic anti-malarials, synthetic drugs which may or may not be administered with quinine, and some nitrogenous bases whose structure is a part of the quinine structure. The object has been two-fold: (1) to provide data for evaluating analytical quinine data when quinine is given impure or jointly with another drug and (2) the application of the quinine method to other substances. The procedure was identical to that of the previous report which described comparatively quinine, quinidine, hydroquinidine, and cinchonine.

Cinchonidine, quitenine, nicotine, strychnine, narcotin, cocaine, thiamin, and novacaine each gave stable silicotungstates and curves similar to and approaching the quinine concentration curve. Caffeine, quinoline, pyridine, antipyrine, and morphine constitute a second group which gives smooth curves but at higher concentrations—the minimal determinable concentrations being approximately 110, 35, 275, 50, and 120 mg. per liter, respectively. Choline, theobromine, pyridoxine, nicotinic acid, and barbital gave no insoluble silicotungstates with standards below 50 mg. per cent. The yellow colors of acid solutions of plasmochin, atabrine, and colchicine render these unadaptable to study by the quinine method. Santonin, riboflavin, and cinchophen yielded no suitable standards for study because of their insolubility. The extractability of the above compounds according to the quinine procedure is mainly completed, continues in progress, and will be reported later.

The metabolism of d-ribose. HARDY W. LARSON, PHOEBE J. BRADSHAW, MARY E. EWING, SUSAN D. SAWYER and N. R. BLATHERWICK. *Metropolitan Life Insurance Company, New York City.* *d*-Ribose, a commercial product conforming to the accepted standards of purity, was given by stomach tube and by intraperitoneal injection to female albino rats weighing from 165 to 200 grams. After a preliminary fast of 24 hours, 2 cc. of a 25 per cent solution of the sugar were administered. Absorption was allowed to proceed for 3 hours when the tissues were removed and analyzed according to the technique of this laboratory.

Increases in liver glycogen occurred after both forms of administration but were significant only after intraperitoneal injection. Simultaneous significant decreases were found in muscle glycogen. Significant decreases in the lactic acid content of liver and muscle and in the fermentable reducing substances of liver, kidney and muscle resulted after oral administration. A significant decrease in blood glucose followed the injection of the pentose. Significant decreases in the non-fermentable reducing substances of muscle and blood were observed after oral administration. The non-fermentable reducing substances of liver and kidney increased significantly after injection. An average coefficient of absorption of 7 mgm. per 100 grams per hour was obtained when 1 cc. of a 25 per cent solution of the sugar was given by stomach tube.

Properties of alfalfa pectinesterase (pectase). HANS LINEWEAVER and GERALD A. BALLOU. *Western Regional Laby., Bureau of Agricultural Chemistry and Engineering, Agricultural Research Administration, USDA, Albany, Calif.* The activities of dialyzed preparations of pectinesterase prepared from alfalfa (and also from other sources) have been found to be increased about 30-fold by the addition of various salts. With 11 inorganic salts, the maximum activity values varied only about 10 per cent; hence activation is apparently not dependent on any specific salt. However, the initial slopes of activity-versus-salt-concentration curves and the optimum salt concentrations depend chiefly on the cations. Initial slopes for Ca, Mg and Mn, and K and Na ions were 20, 7, and 1, respectively, while optimum concentrations of these ions were about 0.025M, 0.05M, and 0.15M. Although the cations may affect either the enzyme, substrate, or both, it is probable that a considerable part of the activation is due to interaction between the cations and pectin. This view is supported by the observation that cations cause a similar but less striking increase in the rate of chemical de-esterification (pH 9.0) of pectin.

At optimum salt concentration a high specific hydrolytic activity (based on equivalents of bonds split per mg. of enzyme protein nitrogen) comparable with that of the crystalline proteolytic enzymes has been obtained. The enzyme de-esterifies pectin at least several hundred times as fast as it does either methyl-α-D-galacturonate or α-methyl-D-galacturonide methyl ester, although all three compounds are de-esterified chemically at nearly the same rate at pH 9.

Antigenic properties of native and regenerated bovine albumin. D. S. MARTIN, J. O. ERICKSON and HANS NEURATH. *Depts. of Bacteriology and Biochemistry, Duke Univ. School of Medicine, Durham, N. C.* Quantitative precipitin measurements were carried out on sera obtained by immunization of groups of rabbits against A, native, carbohydrate-containing bovine albumin; B, the same protein regenerated from 8 *M* solutions of urea, and C, guanidine hydrochloride (Putnam, Erickson, Volkin and Neurath, Fed. Proc. 2: 000, 1943): D, native, crystalline, carbohydrate-free bovine albumin (obtained through the courtesy of the Dept. of Physical Chemistry, Harvard Medical School). Precipitin measurements were carried out to determine 1, the influence of immunizing dose and nature of antigen on the precipitin titer, and 2, the degree of specificity.

The antisera showed such marked variations in antibody titer that the range of doses injected (10 to 80 mgm. protein per kgm. body weight) could not be correlated with the degree of precipitin response. Precipitin titers elicited by injections of antigen C were lower than those produced by antigens A and B, whereas those elicited by antigen D were lower still. Anti-C rabbit sera (average of 24 rabbits) combined optimally with 0.113 mgm. antigen per cc., anti-B sera with 0.274 mgm., anti-A sera with 0.383 mgm., and anti-D sera (6 rabbits) with 0.026 mgm. of homologous antigen. All antigens were immunologically equivalent, and in no instance were anaphylactic reactions observed.

While the presence of carbohydrate in preparations A, B and C may be responsible for their higher antigenicity, it appears significant that for all antigens the antigenicity decreased with increasing susceptibility to tryptic hydrolysis. Regeneration or purification did not impair the antigenic specificity of bovine albumin.

Determination of volatile fatty acids in blood. J. F. MCCLENDON. *Research Laby. of Physiology, Hahnemann Medical College, Philadelphia.* The pyrex still, condenser and trap are united by fusing the glass and the still is filled and emptied through the opening for admitting steam. Ten cubic centimeters of blood are spurted into 50 cc. of 2 per cent zinc sulfate and refrigerated. Twelve cubic centimeters of the top are measured in a pipet and mixed in a centrifuge tube with 2 cc. of *N* NaOH and spun. Seven cubic centimeter of

the clear liquid are mixed in the still with 0.5 cc. of purified syrupy phosphoric acid. The still is immersed in a glycerol bath at 110° while steam is passed through it and 30 cc. of distillate collected in a 50 cc. pyrex erlenmeyer flask. Air (passed through a potash bulb and permutit suspension) is bubbled through the distillate plus 3 drops of 0.04 per cent brom thymol blue for 10 minutes and during the titration. The distillate is titrated with 0.01 *N* CO_2-free NaOH in a buret graduated in 0.001 cc. and tip immersed (in front of a daylight fluorescent lamp and flashed opal diffuser) to the color of a standard flask containing 30 cc. of CO_2 and NH_3-free distilled water plus indicator and 1 mg. of sodium acetate. The titre of 30 cc. of distillate (free from volatile fatty acid) is subtracted from each determination. Quadruplicates can be run as the erythrocytes settle (or are centrifuged). No change has been noted in several days. A battery of 4 stills is run at the same time.

The excretion of vitamin A in dog urine. AGNES FAY MORGAN and LILLIAN S. BENTLEY. *Laby. of Home Economics, Univ. of California, Berkeley.* The excretion of vitamin A in dogs' urine has been studied in the hope that it may be useful in determining the conditions which govern the utilization of beta carotene. Since liver damage produced by heated protein diets may interfere with transformation of carotene into vitamin A such diets were employed in this experiment.

Six young dogs fed heated and raw casein-containing diets were depleted of vitamin A and were found to excrete no vitamin A. Increasing amounts of beta carotene up to 3330 I.U. per kgm. per day were then given the dogs but in no case was urinary vitamin A found. When 13000 I.U. vitamin A in gray fish liver oil was given, the dogs on raw diet excreted vitamin A at once but those on heated diet did not even after 3 to 4 months. Desoxycholic acid was given with carotene and raw diet for 3 months in one case without result but in another, when given with vitamin A and heated diet, after 3 months a small amount of vitamin A appeared in the urine.

Older dogs never depleted of vitamin A, and fed a normal raw casein diet, excreted 1000 to 9000 I.U. per day but young dogs under similar conditions excreted very little. The urinary vitamin A appears therefore to represent a massive accumulation mainly in the liver and this accumulation is dependent upon the intactness of the liver, particularly when carotene is fed. [*Aided by a grant from Swift & Co.*]

Efficiency of aerobic phosphorylation in cell-free tissue extracts. SEVERO OCHOA. *Dept. of Medicine, New York Univ., and Medical Service of the Psychiatric Division, Bellevue Hospital, New York City.* When glucose, creatine, or other phosphate acceptor is added to respiring tissue preparations inorganic phosphate disappears and the acceptor is phosphorylated. This so-called aerobic phosphorylation is proportional to the oxygen consumption. It has been shown with dialyzed brain extracts (S. Ochoa, J. Biol. Chem. 138: 751, 1941) that phosphorylation of either hexose monophosphate or glucose to hexose diphosphate is linked with the oxidation of pyruvic acid, and occurs only in the presence of adenylic acid or adenosine triphosphate (ATP). This is the result of (1) phosphorylation of adenylic acid or adenosine diphosphate to ATP linked with the oxidation, and (2) transfer of phosphate from ATP to the acceptor. Adenosine triphosphatase, which is present in the extracts, interferes with (2); hence the P/O ratio of 2 previously obtained, i.e., 2 atoms of phosphorus esterified for every atom of oxygen consumed, is probably too low.

By comparative measurements of the esterification caused by the dismutation between triose phosphate and pyruvate with that produced by oxidation of pyruvate in cat heart extracts it has now been found that the true value of the P/O ratio of pyruvate oxidation is 3. Thus the complete oxidation of 1 molecule of pyruvate by 2.5 molecules of oxygen can bring about the esterification of 15 atoms of phosphorus.

Comparative hematopoietic values of certain dietary proteins. ALINE UNDERHILL ORTEN and JAMES M. ORTEN. *Dept. of Physiological Chemistry, Wayne Univ. College of Medicine, Detroit.* The effectiveness of different dietary proteins for hemoglobin and erythrocyte formation is being investigated in albino rats fed a synthetic diet. The proteins are fed at two levels, 18 and 2.8 per cent, respectively; the remaining dietary constituents supply adequate amounts of all other known essentials. The hematopoietic value of the various proteins is being determined by (1) their ability to maintain hematopoiesis over an experimental period of 120 days, and (2) their efficacy in promoting hemoglobin and erythrocyte regeneration in hemorrhagic anemia produced by a standardized procedure.

Rats given 18 per cent of protein as lactalbumin showed excellent growth and maintained normal hemoglobin and erythrocyte values, whereas those fed 2.8 per cent of protein grew only slightly and developed a chronic anemia. Animals given 18 per cent of protein as a special mixture of milk and whole blood solids also showed good growth and normal blood values. When this mixture was fed at the 2.8 per cent level, however, gradual loss of weight occurred and a severe anemia developed, followed by death in many animals. The feeding of 18 per cent of protein as beef blood solids resulted in very poor growth and the maintenance of low normal blood values; when fed at the low level,

Inactivation of codehydrogenase I by alkali. F. SCHLENK. *Univ. of Texas, Medical Branch, Galveston, and M.D. Anderson Hospital for Cancer Research, Houston.* It has been shown recently (P. Handler and J. R. Klein. J. Biol. Chem. **143:** 49, 1942) that the inactivation of codehydrogenase I by animal tissues *in vitro* yields, besides nicotinamide, a product which consists of ribosephosphoric acid and adenylic acid (degradation product nr. 1). It has been found in this laboratory that the same compound can be obtained by alkaline hydrolysis. Whereas alkaline hydrolysis at 100° yields adenosinediphosphate and adenylic acid, hydrolysis at 0 to 2° in 0.1 N NaOH for 16 to 20 hours yields 70 to 80 per cent of the degradation product nr. 1 consisting of adenine, 2 mol. of pentose, and 2 mol. of phosphoric acid. In addition, 10 to 15 per cent of adenylic acid or adenosinediphosphate is formed, and 80 to 90 per cent of nicotinamide is liberated. Ten to 15 per cent of codehydrogenase remains unchanged. Prolonged hydrolysis results in further breakdown of degradation product nr. 1.

The isolation may be carried out by fractional precipitation as lead, barium, and silver salts. Obviously, this compound has no codehydrogenase activity. It cannot replace adenosinediphosphate as phosphate transporting coenzyme, since the position which is reserved in the latter for a third phosphoric acid radical is occupied by ribose.

Products of salt-catalyzed hydrogen peroxide oxidation of carbohydrates. FAY SHEPPARD, MARK R. EVERETT and CLIFFORD F. GASTINEAU. *Dept. of Biochemistry, Univ. of Oklahoma School of Medicine, Oklahoma City.* Hydrogen peroxide gave the following products in 1 per cent carbohydrate solution within 30 minutes at 25° C. With 4 molar equivalents of potassium bicarbonate, sugar alcohols gave 2 to 8 per cent aldoses; *d*-fructo-l-uronic acid: 65 per cent non-reducing acids; *d*-glucosamine: an aldose, less uronic acid; *d*-gluconolactone: 23 per cent *d*-arabinose, less *d*-fructo-l-uronic acid, no glucosone or ketose; *d*-mannono-, *d*-gulono- and *d*-galactono- lactones: analogous products; six pentonolactones: 16 to 29 per cent reducing material (aldotetroses, keto-l-uronic acids); *l*-fuconolactone: a keto-l-uronic acid. Uronic acid tests were negative for oxidized *l*-rhamnono-, *d*-glucoheptono- and digitoxono- lactones.

With 0.1 molar equivalent of ferrous sulfate, hexitols gave 50 per cent aldoses, traces of uronic acids and ketoses, no osone; glycerol: 25 per cent glycerose; *d*-glucose: 40 per cent non-fermentable reducing material (partly uronic acid), non-reducing acids; no osone; *d*-fructose: 50 per cent unfermentable ketose, non-reducing acids, no uronic acid; *d*-fructo-l-uronic and *d*-galacturonic acids: 75 and 65 per cent non-reducing acids, respectively; *d*-glucosamine: an aldose; *d*-saccharic acid: 33 per cent unidentified reducing substance; *d*-gluconolactone: 22 per cent *d*-arabinose, 12 per cent keto-l-uronic acid and keto derivatives, non-reducing acids, no osone; other hexonic lactones: analogous products; pentonic lactones: 21 to 38 per cent reducing material (aldotetroses, keturonic acids).

With 2 molar equivalents of cupric sulfate, hexitols gave 20 per cent reducing material (mostly ketoses, no uronic acid); *d*-glucose: 10 per cent uronic acid, glucosone (fermentable by Somogyi technique); *d*-gluconolactone: 34 per cent reducing material (15 per cent keturonic acid, alduronic acid, aldose, no ketose or osone).

Composition of blood and bone in relation to diet. ALBERT E. SOBEL, MORRIS ROCKENMACHER and BENJAMIN KRAMER. *Pediatric Research Laby., The Jewish Hospital of Brooklyn.* The inorganic composition of bone may be expressed as $[Ca_3 (PO_4)_2]_n \cdot CaCO_3$ where n is between 2 and 3. It has been observed that n decreases with age, in rickets and in a pathological condition called "marble bones" (osteopetrosis).

In our experiments an attempt was made to interrelate the variation of n to the ratio of serum calcium to inorganic phosphorus. This ratio is influenced by the dietary calcium and phosphorus. It was found that the bones of rats fed high calcium low phosphorus diets had significantly higher carbonate to phosphate ratios than the bones of rats on high phosphorus low calcium diets. The rats receiving vitamin D supplements had denser bones, but the carbonate to phosphate ratio in the bones was similar to those not receiving this supplement.

The ratio of serum calcium to inorganic phosphorus was higher in the high calcium fed group than in the high phosphorus fed group. These differences prevailed in the vitamin D fed rats but were less marked. The serum Ca x P products, however, were higher, explaining the increased density of the bones.

It was suggested that the dietary calcium-to-phosphorus ratio influences the carbonate to phosphate ratio of the bones. These results may be explained in part, by the serum calcium, inorganic phosphorus and carbonate levels obtained.

Brain phosphatidase. WARREN M. SPERRY. *Depts. of Biochemistry, the New York State Psychiatric Inst. and Hospital and Columbia Univ., New York City.* A decrease in the total phosphorus extracted by lipid solvents during incubation of emulsions of rat brain tissue in saline carbonate buffer for 4 hours was described in a recent report (Proc. Div. Biol. Chem., Amer. Chem. Soc., B5, Buffalo, 1942). Further study of this effect yielded the following results: (a) A somewhat larger change was usually observed when the time of incubation was increased to 20-24 hrs. (as in all the experiments reported here). (b) No con-

sistent effect of shaking in the Warburg apparatus during the first 5–6 hours of incubation could be demonstrated; in the majority of cases shaking appeared to exercise an adverse influence. (c) The magnitude of the decrease in extractible phosphorus was diminished, usually by over half, by heating the emulsions in boiling water for 5 min., or at 60° for 1 hr. Complete inactivation usually, though not always, followed heating in boiling water for 10 min. (d) The response in 5 day old rats was the same as in adult rats. (e) The effect was usually greater in emulsions made in Krebs' carbonate solution than in a solution containing NaCl and carbonate only, but the difference was not statistically significant. (f) Emulsions made in water showed no activity; a result which suggests that intact cellular structures are necessary for phosphatidase action. (g) Brain tissue which had been ground to a paste in a mortar and suspended in saline carbonate buffers gave the same result as did the emulsions.

X-ray diffraction studies on urea-treated proteins. MONA SPIEGEL-ADOLF and GEORGE C. HENNY. *Depts. of Colloid Chemistry and Physics, Temple Univ. School of Medicine, Philadelphia.* Former attempts were continued to analyze the effects of heat, short-wave light, x-rays, alcohol, etc., upon different kinds of proteins by x-ray diffraction methods. To this purpose our studies were extended in the action of urea upon serum albumin and pseudoglobulin.

In a preliminary investigation it was shown that the amount of protein which loses its water solubility after 24 hours of contact with urea of 6.66 M varies with the kind, concentration, and pH of the protein used. After protracted dialysis and electrodialysis (N. F. Burk, J. Biol. Chem. 98: 353, 1932) pseudoglobulin as well as albumin could be separated into a water soluble and a water insoluble fraction. After drying and pulverization of these fractions x-ray diffraction studies were made with the following results:

All water-soluble fractions showed the patterns of undenatured proteins while the insoluble ones were characterized by a marked sharpening of the back-bone reflection. The latter findings confirm previous results of Astbury. Upon treatment of the water-insoluble urea-treated albumin fraction with alkali, subsequent neutralization, purification, and drying, the sharpening of the backbone reflection disappeared. No such reversal of the changes in the x-ray diffraction pattern of water-insoluble urea-treated pseudoglobulin could be elicited by an analogous treatment. The similarity of these findings with changes observed in heat-denatured proteins is obvious. (J. Phys. Chem. 45: 931, 1941). Studies are under way to ascertain how far the reversibility of the changes in the x-ray diffraction pattern correspond to changes in other physico-chemical properties of urea-treated serum albumin.

Determination of atabrine in tissues. ELMER STOTZ, J. M. MCKIBBIN, D. M. HEGSTED and F. J. STARE. *Schools of Medicine and Public Health, Harvard Univ., Boston.* Atabrine can be extracted from tissue suspensions by certain organic solvents and its acid salt returned to aqueous solution. A yellow color and a fluorescence serve for its estimation.

A 1 to 4 ml. sample of tissue homogenate (0.25 g./ml.) is treated with 2 ml. of 10 per cent sodium desoxycholate and 5 to 6 drops of 40 per cent KOH to obtain a colloidal dispersion. Extractions with successive 10 ml. portions of ethyl ether are performed by passing a stream of air into the mixture through a capillary tube. The combined ether extract is evaporated to 1 to 2 ml. Ten ml. of petroleum ether is added, followed by extraction with two 5.0 ml. portions of 2 N. HCl. A white precipitate, if it occurs, may be filtered off.

The atabrine is determined with the photoelectric spectrophotometer at $\lambda = 430$ mμ if the solution is colored. If colorless, the fluorescence is measured in a fluorometer using "riboflavin" filters, 1 microgram of atabrine giving a deflection of approximately 10 divisions. Standard atabrine solutions are prepared in 2 N. HCl. Added atabrine, from 1 to 100 micrograms, is recovered in 85 to 100 per cent of theory. Tissue atabrine values per unit weight of tissue are independent of the amount of tissue used for analysis. A variable blank fluorescence from the tissues can be estimated on the same analytical sample by subsequent addition of a drop of 1-to-1000 bromine water which rapidly destroys the atabrine fluorescence without affecting the blank fluorescence.

***l*-amino acid oxidase of proteus vulgaris.** P. K. STUMPF and D. E. GREEN. *Depts. of Medicine and Biochemistry, College of Physicians and Surgeons, Columbia Univ., New York City.* Proteus vulgaris contains an enzyme which catalyses the oxidative deamination of some twelve *l* amino acids. One atom of oxygen is consumed for each molecule of amino acid deaminated, and the product formed is the corresponding keto acid. The 2,4-dinitrophenylhydrazones of the ketoacids of tryptophane, methionine, leucine, norleucine, valine, norvaline, tyrosine, isoleucine and phenylalanine have been isolated and identified. The enzyme can be extracted from the cell by exposing the bacterial suspensions to sonic vibrations, centrifuging off and discarding insoluble material. The cell-free soluble enzyme is stable during purification by salt fractionation.

The Proteus enzyme attacks only the *l* forms of the amino acids. Phenylalanine, methionine, norleucine, leucine, tyrosine, tryptophane and norvaline are the most active substrates; valine,

isoleucine and histidine are less active whereas arginine and alanine are still less active. The dicarboxylic and the diamino amino acids (arginine excepted), proline, hydroxyproline, glycine and β-alanine are attacked immeasurably slowly if at all.

Oxygen can be replaced by hydrogen acceptors such as methylene blue. The reaction with molecular oxygen is cyanide-sensitive but the cytochrome system is not involved. The purified enzyme preparation has been found to contain bound flavinadenine dinucleotide.

The equivalent of the Proteus *l* amino acid enzyme has been found in other bacteria such as Aerobacter aerogenes and B. pyocyaneus but not in B. coli, haemolytic Streptococcus and others. The Proteus *l* enzyme differs from its analogue isolated from rat kidney and liver in that it is sensitive to capryl alcohol and relatively insensitive to ammonium ions.

Effect of 2-methyl-1,4-naphthoquinone on the metabolism of isolated animal tissues. WILLIAM H. SUMMERSON. *Dept. of Biochemistry, Cornell Univ. Medical College, New York City.* In the presence of 2-methyl-1,4-naphthoquinone at a concentration of approximately 1x 10^{-4} M., rabbit exudate leucocytes respiring in Ringer-bicarbonate-glucose medium show an inhibition of aerobic lactic acid production of 50 per cent or more. At the same time, there is a 10–15 per cent increase in the rate of oxidative metabolism, and a slight rise in R.Q. Rabbit bone marrow slices show the same general effect. Rat liver slices show an increased oxygen uptake and a decreased utilization of lactate, but no significant change in R.Q.

Anaerobically, the conversion of added glucose to lactic acid by leucocytes is completely inhibited in the presence of the methyl naphthoquinone, but the endogenous glycolysis of both leucocytes and liver is not affected.

The effect of the methyl naphthoquinone is not sustained, falling off with time. This may be due to inactivation by combination with cell proteins, presumably through the —SH groups present, since the deep yellow protein-methyl naphthoquinone complex obtained from leucocytes is spectrophotometrically very similar to the yellow compound formed when the quinone reacts with cysteine under similar conditions. The possible relation between the action of the methyl naphthoquinone on cell metabolism and its ability to react with compounds containing the —SH group under physiological conditions is being studied further.

The proteolytic and amylolytic enzyme systems of soybeans. HENRY TAUBER and STEPHEN LAUFER. *Research Dept., Schwarz Laboratories, Inc., New York City.* By extraction of defatted soybean with 4 volumes of 30 to 50 per cent glycerol for 24 hours at 30°C. a fairly active proteolytic enzyme system was released. Germination from 6 to 12 days resulted in a very considerable increase in proteolytic activity. The proteinase was activated by sodium sulphite indicating that it is a papainase. The optimum pH of the proteinase is 6.78 with casein, and 7.20 with gelatin as substrate, using sodium citrate as buffer. We propose the name "Soyin" for this proteinase.

Soybeans are one of the best beta-amylase sources. They are known to contain only a trace of alpha-amylase. We found, however, that by extraction with 30 per cent alcohol and fractional precipitation of the filtrate with 95 per cent alcohol a preparation could be obtained that showed in addition to high beta-amylase, fair alpha-amylase activity. Our observations were similar with barley, which is known to be free or almost free from alpha-amylase. We found that soybeans differ from barley in that they do not contain bound beta-amylase. We also confirmed the observation made by others to the effect that soy beans produce only a trace of alpha-amylase during germination. The optimum pH of soy beta-amylase is 5.9 with sodium citrate as the buffer. A quantitative study of various amylase sources has been made.

Xanthopterin and vitamin M deficiency in monkeys. JOHN R. TOTTER, CARROLL F. SHUKERS, JACK KOLSON, VIRGINIA MIMS and PAUL L. DAY. *Univ. of Arkansas Medical School, Little Rock.* Five rhesus monkeys were fed vitamin M-deficient diets as previously described (W. C. Langston *et al.*, J. Exper. Med. 68: 923, 1938), adequately supplemented with ascorbic acid, thiamin, nicotinic acid and riboflavin. As additional daily supplements, two animals received 100 mgm. of inositol, 50 mgm. of choline, 25 mgm. of p-aminobenzoic acid, 1 mgm. of pyridoxine and 10 mgm. of Ca pantothenate; one received 25 grams of banana, and one 20 grams of fresh beef; the fifth received 3 grams of liver powder, prepared by heating fresh liver in an oven at 100°C. for 24 hours (the equivalent amount of untreated liver is fully protective). All animals eventually developed cytopenia. After the inadequacy of each supplement was amply demonstrated, four of the animals were given synthetic xanthopterin in daily doses of 2.5–10 mgm. This therapy resulted in reticulocyte responses of 1.5–4.5 per cent (usual reticulocyte range, 0.2–0.4 per cent) in 3–6 days, which lasted 2–5 days. White and red cell counts increased to normal in 3–13 days and remained normal for varying periods. Only in the animal receiving heated liver did the xanthopterin appear to restore hemocytopoietic function for an extended period. After 71 days the white and red cell counts were still normal and cessation of xanthopterin therapy resulted in a prompt return of the cytopenia.

Resumption of xanthopterin feeding elicited a second response similar to the first.

The results suggest that xanthopterin is required by the monkey for hemocytopoiesis, but unidentified substances are also necessary to prevent vitamin M deficiency. [*Aided by grant from the National Research Council Committee on Meat Board Grants.*]

Growth, reproduction and lactation in several generations of rats maintained on highly purified diets. LEONARD J. YINSON and LEOPOLD R. CEREDO. *Dept. of Chemistry, Fordham Univ., New York City.* Growth, reproduction and lactation on highly purified diets were studied on two strains of rats, Wistar and Long-Evans, through several generations. The basal ration had the following percentage composition: Purified casein, 30; salt mixture, 5; Ruffex, 2; lard or Crisco, 10 (or a combination of both, 15); and sucrose, to make 100 per cent. This ration was supplemented with the following vitamins, added per kilo of diet: thiamin, 20 mgm.; Riboflavin, 20 mgm.; pyridoxine, 20 mgm.; pantothenic acid, 40 mgm.; choline chloride, 500 mgm.; alpha-tocopherol, 20 mgm.; and vitamin A and D concentrate, 40 mgm.

The Wistar rats have been raised through four generations on this ration. The growth rate of these animals was at least as good as that of the controls kept on Purina dog chow. In many instances, it was observed to be even superior. The growth of the fourth generation rats compared favorably with that of the first generation. Of a total of 52 litters born, 33, representing 188 young, were successfully weaned.

Similar results were obtained with the Long-Evans rats, four generations having been raised. The growth of these animals was better than that of the controls on Purina dog chow. Nineteen litters were born, of which 12, totaling 75 young, were weaned.

An interesting observation has been made in both strains: invariably during lactation the mothers lost considerable weight, which, however, was regained when they were separated from their young after weaning.

THE AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS

Abstracts of papers presented for the annual meeting scheduled for Cleveland, April 6–10, 1943. On account of the cancellation of this meeting, all the papers are to be regarded as "read by title." For possible correction in any of the abstracts see the next issue.

Influence of morphine and 1-methyl-4-phenyl piperidine-4 carbonic acid ethyl ester HCl (demerol) upon the uterine contribution to the intra-uterine pressure of hypertonic and normal uteri of pregnant humans at various periods of gestation. B. E. ABREU, R. A. WOODBURY and (by invitation) P. H. FRIED and R. TORPIN. *Depts. of Physiology and Pharmacology and Obstetrics and Gynecology, Univ. of Georgia School of Medicine, Augusta.* Pressures were determined by techniques previously described (Am. J. Physiol. 121: 640, 1938).

At three months gestation a balloon and catheter were inserted into the uterus to produce therapeutic abortion. Eight hours later the pressures between contractions had increased from 5 to 9 mm. Hg and during contractions from 7 to 15 mm. Hg. Introduction of 100 cc. fluid into the balloon elevated the uterine tone so that pressures were 22 mm. Hg between and 29 mm. Hg at the height of contractions. This hypertonic, hyperactive uterus is similar to those of patients threatening to abort. Morphine sulfate 10 mgm., i.v., practically eliminated contractions and reduced the tone so that the pressure was 12 mm. Hg, even though the uterus still contained the distended balloon. Similar studies later with demerol in the same patient showed that analgesic dosages (100 mgm.) failed to significantly decrease uterine tone and activity.

In other patients at 3 and 8 months gestation, when the introduction of fluid into the balloon had only slight effects upon the uterine activity and tone, single doses of either morphine or demerol produced no significant uterine changes.

At 8 months gestation, the uteri of two other patients were rendered hypertonic and hyperactive by administration of pitocin to one and ergotrate to the other. Morphine sulfate 8 mgm., i.v., reduced frequency 25 per cent, tone 33 per cent and pressure at the height of contractions 27 per cent. Demerol 100 mg., i.m., had no significant effect upon uterine tone or activity.

Morphine and demerol relax skeletal muscles and thus reduce the abdominal contribution to the intra-uterine pressure. For the adequate evaluation of drug action upon uterine activity, it is

essential that the uterine and abdominal contributions be separated from each other. [*This work was aided by a grant from Eli Lilly and Company.*]

Toxicological and pathological studies on alpha naphthyl isothiocyanate. A. M. AMBROSE and A. J. MILLER (by invitation). *Depts. of Pharmacology and Pathology, Univ. of Louisville School of Medicine, Louisville, Ky.* The acute and chronic toxicity of alpha naphthyl isothiocyanate has been studied for young and adult albino rats. For acute toxicity the drug was dissolved in vegetable oil and the solution was administered by gavage to 4 groups of 10 rats each, and subcutaneously to 4 groups of 10 rats. The doses employed were 0.1, 0.2, 0.4 and 0.8 gram/kgm. The percentage mortality was 10 per cent after 0.1 gram/kgm. orally and 20 per cent after 0.2 gram/kgm. subcutaneously.

For chronic studies 8 groups of 5 female rats weighing 45 to 49 grams each at weaning were used. One group served as the control and was placed on the basic diet, the composition of which has been previously reported (Ambrose. J. Pharmacol. 76: 245, 1942) and the remaining groups were placed on the basic diet which contained 0.0078, 0.0156, 0.0312, 0.0625, 0.125, 0.25 and 0.5 per cent alpha naphthyl isothiocyanate. The experiment lasted 105 days. In concentrations of 0.125 to 0.5 per cent the rats refused to eat and died. In concentrations of 0.0625 per cent there was a slight decrease in growth rate and food consumption as compared to controls. In the lower concentrations growth rates and food consumption was not significantly different from that of the controls.

In another series 4 groups of 5 female rats were placed on the diet containing 0.0625 per cent of the drug for 4, 7, 14 and 28 days.

Histological studies of all rats receiving the drug continuously showed moderate to severe cirrhosis of the liver dependent upon the concentration of the drug in the diet and the duration of exposure to the contaminated food. The damage was permanent and irreparable since withdrawal of the contaminated food after 105 days and replacing it with the control diet for an additional 60 days showed no evidence of recession or healing. All other organs were indistinguishable from those of the untreated controls.

Reversible binding of atropine by rabbit's tissues and blood. R. BEUTNER. *Dept. of Pharmacology, Hahnemann Medical College, Philadelphia.* Previous investigations (Beutner. J. Pharmacol. 25: 365, 1925) (Beutner and Hyden. J. Pharmacol. 35: 27, 1929) have shown that rabbit serum binds atropine without entirely decomposing it since the unaltered alkaloid can be recovered from an alkaloid-serum mixture by diffusion through paper after addition of ether, etc. But without ether addition atropine in small amounts is prevented from diffusing by serum protein. This binding would account for the refractoriness of rabbits to atropine poisoning. LaBarre (J. Pharmacol. and Exper. Therap. 26: 259, 1925) had contested this finding maintaining that atropine was entirely decomposed in the liver.

A search of the literature, for which the writer is much indebted to Dr. J. R. Comroe of the University of Pennsylvania, revealed a case report of typical atropine poisoning after the eating of rabbit meat from an animal which had fed on Belladonna leaves (Firth and Bentley. Lancet 2: 901, 1921). Obviously, this poisoning would not have been possible if atropine had been completely decomposed, as contended by LaBarre. Another similar case report on atropine poisoning is available (H. H. Selye. Med. Record 45: 14, 1894), but here turkey meat was ingested; obviously the tissue of these birds have also the faculty of binding atropine. Decomposition slowly follows after the binding (V. D. Heyde, 1921).

The excretion of orally administered orthonitrophenol. R. BEUTNER and R. BLOCK (by invitation). *Dept. of Pharmacology, Hahnemann Medical College, Philadelphia.* Beutner and Cohen (Federation Proc.) showed that o-nitrophenol can be recovered from the urine of rabbits after intramuscular injection almost 100 per cent. In view of the possible use of nitrophenol as a urinary antiseptic we administered it by stomach tube to 3 rabbits (the dose being 1.1 to 1.3 grams) as 2 per cent solution. The urine was collected over a period of 19 hours and, after acidification with 50 per cent H_2SO_4, subjected to steam distillation until clear water came over. The distillate, which contained all the nitrophenol, was alkalinized until it turned deep yellow. Its nitrophenol content was determined by colorimetric comparison with a 2 per cent alkaline nitrophenol solution. The amounts of nitrophenol thus determined in the distillate were: 687.8 mgm., 656.2 mgm. or 853.7 mgm., corresponding to 52.6 per cent, 57.0 per cent or 77.5 per cent of the amounts fed to the animals. The average nitrophenol concentration in the excreted urine was 0.25 per cent. No other phenol derivative is excreted as completely, according to other investigations in this laboratory. Orthonitrophenol is, moreover, non-toxic and without any influence on metabolism, in contrast to dinitrophenol (see Federation Proc. 1).

The effect of alkalinization and acidification on local anesthetics. R. BEUTNER and P. A. BRADLOW (by invitation). *Dept. of Pharmacology, Hahnemann Medical College, Philadelphia, Pa.* As is known, the addition of alkali to local anesthetic solutions increases their potency, but this does not hold for hydrochlorides of such anesthetic bases as nupercaine and pontocaine. Addition of a small amount of $NaHCO_3$ diminishes anesthetic

potency because of precipitation of the anesthetic as insoluble base, while procaine or butyn base are relatively more soluble. Acidification invariably diminishes anesthetic power by inhibiting the liberation of the anesthetic base. In the case of nupercaine these changes are extremely large as the following observations show:

Into the eye of 3 rabbits was instilled and held there for 15 seconds:	pH	The anesthesia lasted:
0.3 cc. 1% nupercaine HCl	3.3	4000 min. (2¾ days)
0.3 cc. 1% nupercaine HCl + $NaHCO_3$ (1:2000)	6.0	246 min. (4 hrs. 6 min.)
0.3 cc. 1% nupercaine HCl +HCl (1:1000)	1.8	190 min. (3 hrs. 10 min.)

In another set of experiments Beutner and Calesnick had previously described a similar very marked diminution of the anesthetic potency of nupercaine after $NaHCO_3$, the duration of anesthesia (after 0.3 cc. held for a shorter time) dropping from 3000 minutes to 132 (Anesthesiology 3: 675, 1943). But, now, we see that anesthesia is very markedly shortened after slight acidification also. Also pontocaine (tetracaine USP XII) and diothane showed a diminution of anesthetic potency after acidification *or* alkalinization, although to a much slighter extent, but *procaine* or *butyn* only after acidification. The duration of anesthesia was 110 minutes for pontocaine without addition (9 animals), dropping to 57 or 73 after alkali or acid; 125 for diothane (6 animals), dropping to 90 and 42 respectively.

Vitamin B deprivation and spontaneous activity in white rats. A. L. Bloomfield and M. L. Tainter. *Depts. of Medicine and Pharmacology and Therapeutics, Stanford Univ. School of Medicine, San Francisco.* Ten littermate pairs of rats were placed in revolving cages, and food consumption, weight and voluntary running were recorded daily. After a three weeks control period on normal diet half the rats were changed to a B-free diet. As they lost weight, the controls were kept at the same weight level as the deficient rats by restriction of their food intake. The B-deficient rats became hyperexcitable and ran more during the first ten days of deprivation. A second series was run similarly using a B-free diet throughout and supplying whole B-complex separately. On withdrawal of the vitamin from half the animals, the same sequence of transient hyperexcitability occurred. Food limitation without reduction of the B intake did not modify the spontaneous activity. When the vitamin was restored and unlimited food intake permitted, the animals gorged themselves for several days and stopped running almost entirely until a new dietary equilibrium was established. Therefore, vitamin B deprivation in the rat is associated in the early stages with increased spontaneous activity and hyperexcitability.

An antibacterial substance produced by an Aspergillus flavus. Milton T. Bush and Andres Goth (by invitation). *Dept. of Pharmacology, Vanderbilt Medical School, Nashville, Tenn.* A mold of the Aspergillus flavus group was isolated and found to produce substances which dissolve Gram positive cocci and inhibit the growth of a number of pathogenic bacteria. The bacteriostatic substance *aspergillin* is produced by growing the mold on a modified Czapek-Dox medium. *Aspergillin* was extracted with isopropyl ether from the acidified culture filtrates. Following partial purification a solid material was obtained which inhibited the growth of Staphylococcus aureus and Staphylococcus albus at a dilution of 0.008 mgm./cc. of broth. Streptococcus hemolyticus, Pneumococcus, C. diphtheriae, B. anthracis were inhibited at a dilution five times as great. Brucella abortus, Eberthella typhosa, Dysentery bacilli, V. cholerae, and B. subtilis are also inhibited at higher concentrations. E. coli, P. pestis, B. Friedlanderi were not inhibited at a concentration of 0.8 mgm./cc. The partially purified *aspergillin* has a median lethal dose of about 40 mgm./kgm. when administered intraperitoneally to mice. Further purification of the antibacterial substance is under way, and we have good evidence that the activity-toxicity ratio can be further increased.

The protective value of sorbitol-gelatine films against Lewisite vapors and liquid. C. Jelleff Carr. *Dept. of Pharmacology, School of Medicine, Univ. of Maryland.* The complex formed when a sugar alcohol, such as sorbitol, is heated with gelatine has found wide industrial application. The physical and chemical properties of this substance and the gas impermeable character of the films of this complex suggested the determination of its prophylactic value against chemical warfare agents and industrial chemicals and solvents. Large rabbits used in these experiments were exposed to standard quantities of Lewisite vapors and liquid. One half of the abdominal area was covered with the protective film. Each animal served as its own control as the unprotected area was scrubbed with soap and water. The protection against Lewisite provided by these films far exceeds in value the protection afforded by washing with strong soap and water alone *after* the period of exposure. The use of this material by workers exposing themselves to Lewisite offers a decided advance in routine prophylaxis. The value of washing with soap and water alone after exposure to Lewisite has been amply demonstrated in these experiments. It is suggested that these films provide a water soluble, mechanical barrier to the passage of vesicant vapors or liquid. Pre-

liminary experiments on humans indicate that these films are protective also against dichlorethyl sulfide liquid.

The effect of digitalis glycosides on potassium metabolism. McKeen Cattell. *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* Earlier experiments have demonstrated an action of the digitalis glycosides resulting in a loss of potassium by isolated striated muscle from the frog, and more recently it has been shown by Visscher that the tissues of the heart-lung preparation of the dog respond similarly. The present experiments were carried out on normal dogs with a view to determining whether ouabain, in doses which could be regarded as within the therapeutic range, causes changes in potassium metabolism. Female dogs were kept without food and daily determinations made of the blood concentration and urine excretion rate of potassium. After 3 or 4 control days from 0.3 to 0.5 mgm. per kilo of ouabain was given by a single intravenous injection, following which hourly specimens of urine obtained by catheter were examined. The potassium excretion was uniformly high during the first few hours after ouabain. In seven animals the excretion rate, expressed in mg. of potassium per kilo per hour, rose from an average control value of 2.7 to 6.2 during the period of from 6 to 9 hours immediately following the ouabain injection. On the following day the excretion rate was markedly reduced, averaging only 0.7. In a majority, but not all of the animals there was a moderate rise in blood potassium (4 to 8 mgm.) during the first few hours after ouabain.

The effects of some new antispasmodics on the bronchial musculature of perfused guinea pig lungs. H. F. Chase (by invitation), A. J. Lehmann and F. F. Yonkman. *Dept. of Pharmacology, Wayne Univ., Detroit.* The bronchodilator action of some new antispasmodic morpholine derivatives has been tested using the method of Sollman and Von Oettingen for bronchial perfusion of guinea pig lungs as modified by Tainter, Pedden and James. The ability of these drugs to relax bronchial smooth muscle was determined on fresh, untreated lungs and on lungs whose bronchi had been previously constricted by histamine. Comparisons were made with epinephrine and Trasentin. The ratio of the percentage recovery to the effective dose was computed for all drugs and expressed on the basis of epinephrine having an arbitrary value of 100. With this standard, the morpholine compounds and Trasentin ranged in their antispasmodic action as follows:

Epinephrine	100.0
Trasentin β Diethylaminoethyl diphenylacetate hydrochloride	9.4
S-29 ω (4-Morpholine)-hexyl diphenylacetate hydrochloride	9.0
S-19 β (4-Morpholine ethoxy)-ethyl diphenylacetate hydrochloride	4.0
S-14 β (4-Morpholine)-ethyl diphenyl chloroacetate hydrochloride	3.6

S-29 is the most active bronchodilator of the group of new synthetics studied. Since S-29 from previous studies in our laboratory, was found to be approximately one-half as toxic as Trasentin and is of the same order of antispasmodic activity it would seem to merit clinical trial.

Studies on the chemistry and pharmacology of raspberry (Rubus idaeus) leaves. Maynard B. Chenoweth and Walter Modell (introduced by McKeen Cattell). *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* A sesquiterpene oil has been obtained by steam distillation of an ether extract of raspberry leaves in a yield of about 0.0001 per cent. The oil is yellow, spicy, boiling at 309.1°C. (corr.) at 760 mm. Hg and solidifying at −7.5°C. The specific rotation is $[\alpha]_D^{30.7} = +2.6°$. Very dilute solutions (1:100,000) relax strips of isolated cat uterus, but the substance is very toxic *in vivo* and has no specific effect on the uterus when administered intravenously.

A pharmacologically active substance, the presence of which was indicated by Burn and Withell (Lancet 2: 1, 1941), has been obtained by extraction of the dried leaves, first with alcohol, then with ether (steam-distilled for oil and discarded) and final reextraction with hot water. The aqueous extract is purified with basic lead acetate, the excess removed as lead ortho-phosphate. The resultant solution when administered intravenously to cats, actively relaxes the uterus. The systolic blood pressure is elevated for from 2 to 10 minutes while the diastolic pressure remains unchanged; the pulse pressure is markedly increased.

This solution gives no positive alkaloid reactions and it cannot be further concentrated by the usual methods for alkaloid extraction. The pharmacological effects persist after solutions have been treated with heat, acid or alkali, but combustion of active solutions leaves an inactive ash. Water, ethanol, pyridine and propylene glycol are the only solvents found which will extract an active solution.

The toxicity of chlorophenols for rats. Wm. Deichmann. *Kettering Laby. of Applied Physiology, College of Medicine, Univ. of Cincinnati, Cincinnati, O.* Lethal oral and subcutaneous doses of the chlorophenols produce the same signs of poisoning in rats. Oral administration, however, results in fatal poisoning in smaller dosage and in a shorter period of time.

Restlessness and an increased rate of respiration appear a few minutes after administration of *o*- and *m*-chlorophenol and are followed a few minutes later by a rapidly developing motor weakness. Tremors, clonic convulsions (which can be in-

duced by noise or by touch), dyspnea and coma set in promptly and continue until death. *p*-Chlorophenol produces similar signs but the convulsions are more severe. 2,4-Dichlorophenol and 2,4,5-trichlorophenol produce these signs also, but decreased activity and motor weakness do not appear quite so promptly. The tremors are much less severe, but in this case also, they continue until a few minutes before death. Tetrachlorophenol takes an intermediate place between the lower homologues and pentachlorophenol. The signs it produces are similar to those caused by the lower hydrocarbons except that tremors and convulsions are absent until the terminal stage of poisoning. Pentachlorophenol produces marked hyperpyrexia, which is not seen in animals treated with any of the other chlorophenols. It also causes motor weakness, collapse and terminal asphyxial convulsions.

The lethal dosages of these compounds (LD_{50}) are as follows: *o*-chlorophenol, as a 50 per cent solution in olive oil, 0.67 gm/kgm. orally and 0.95 gm/kgm. subcutaneously; *m*-chlorophenol, as a 20 per cent solution in olive oil, 0.57 gm/kgm. orally and 1.39 gm/kgm. subcutaneously; *p*-chlorophenol, as a 25 per cent solution in olive oil, 0.67 gm/kgm. orally, and as a 50 per cent solution, 1.03 gm/kgm. subcutaneously; 2,4-dichlorophenol, as a 20 per cent solution in fuel oil, 0.58 gm/kgm. orally and 1.73 gm/kgm. subcutaneously; 2,4,5-trichlorophenol, as a 20 per cent solution in fuel oil, 0.82 gm/kgm. orally and 2.26 gm/kgm. subcutaneously; tetrachlorophenol, as a 4 per cent solution in fuel oil, 0.14 gm/kgm. orally and 0.21 gm/kgm. subcutaneously; pentachlorophenol, as an 0.5 per cent solution in fuel oil, 0.03 gm/kgm. orally, as a 1 per cent solution in olive oil, 0.08 gm/kgm. orally, and as a 4 per cent solution in fuel oil, 0.10 gm/kgm. subcutaneously.

The detoxification of phenol. Wm. Deichmann. *Kettering Laby. of Applied Physiology, College of Medicine, Univ. of Cincinnati, Cincinnati, O.* So far as is known, the body has two general mechanisms for the disposal of phenol aside from excretion,—(1) conjugation with sulfuric, glucuronic and possibly other acids, and (2) oxidation. Small amounts of phenol such as are produced by decomposition of proteins in the intestinal tract, are rapidly conjugated and excreted. (Human urine contains from 0 to 4 mgm. of free and from 10 to 40 mgm. of conjugated phenol per day, rabbit urine from 0 to 0.4 mgm. of free and from 1 to 10 mgm. of conjugated phenol.)

When the conjugating mechanism is overwhelmed, as for instance after the ingestion of large amounts of phenol, oxidation of phenol also occurs. The fate of a toxic but sublethal oral dose of phenol in the rabbit is as follows: From 59 to 88 per cent of the phenol is excreted in the urine during the first 24 hours. About half of this amount is present as free phenol; of the conjugated fraction, about half is conjugated with sulfuric acid, a little more than one-fourth with glucuronic acid, and the remaining portion with other acids not yet identified. From 10 to 40 per cent of the phenol is broken down. The bulk is oxidized to carbon dioxide and water, while small amounts are oxidized to pyrocatechol and hydroquinone. Traces of these last two compounds are broken down in the body to dark colored substances, traces are excreted unchanged with the urine, while the bulk is conjugated and then excreted. On exposure to air, the conjugated compounds hydrolyze and pyrocatechol and hydroquinone undergo a further change, with formation of colored substances giving the urine its "smoky" appearance. Traces of free and conjugated phenol are excreted in the feces, and faint traces of free phenol are excreted with the exhaled air. From 2 to 5 per cent of the phenol is still found in the tissues at the end of the first day.

Effect on the systemic venous pressure of digoxin and ouabain administered intravenously to patients with congestive heart failure. Ludwig W. Eichna and Harry Taube (introduced by Arthur C. DeGraff). *Dept. of Therapeutics, New York Univ. College of Medicine, and Third (New York Univ.) Medical Division, Bellevue Hospital, New York City.* It is generally assumed that the recovery of circulatory compensation with the accompanying fall in venous pressure is rather a slow process. However, we persistently encountered a rapid fall of venous pressure when the purified glycosides, ouabain and digoxin, were administered intravenously to patients in congestive heart failure with or without associated disturbances in rhythm.

Determinations of the venous pressure, ventricular rate, arterial tension, electrocardiographic changes, and the rate of flow of urine were made frequently, often simultaneously, throughout a control period and for 2 to 4 hours after injection of the glycoside.

Fourteen patients were given digoxin in doses ranging from 0.5 to 2.5 mgm. Ouabain was given five times in amounts from 0.375 to 0.75 mgm.

The fall in venous pressure had the following characteristics:

a. Onset of effect; ouabain, 3 to 11 minutes; digoxin, 5 to 22 minutes.

b. Maximum effect; ouabain, 35 to 56 minutes; digoxin, 45 minutes to 3 hours.

c. It was associated with, but not dependent on, a slowing of ventricular rate in auricular fibrillation.

d. It was unaccompanied by a change in ventricular rate in regular sinus rhythm.

e. It preceded the onset of diuresis, which, at times, was rapidly initiated.

f. Its pattern did not depend on the initial level of venous pressure or the degree of congestive heart failure.

g. It bore no relationship to changes in the electrocardiogram.

h. Its duration was relatively short, except in those patients whose cardiac reserve was sufficient to maintain circulatory compensation once it was reestablished.

Compared molecule for molecule, ouabain induced effects more rapidly than digoxin.

Bacteriostatic effect on Eberthella typhosa of bile from dogs treated with chloroacetate. G. A. EMERSON and JACK K. FINNEGAN (by invitation). *West Virginia Univ. School of Medicine.* Morrison (U. Calif. Publ. Pharmacol. 1: 397, 1941) found that 0.01 per cent monochloroacetic acid inhibits growth of several micro-organisms. This agent is also a potent choleretic. The closely related tribromoacetate occurs in cystic bile to ca. 0.02 per cent 1 hour after intramuscular injection (J. Pharmacol. 75: 226, 1942). 0.005 per cent chloroacetic acid is said by Tetsumoto (J. Agric. Chem. Soc., Japan 12: 184, 1936) to inhibit growth of typhoid bacilli in vitro. This concentration may be easily surpassed in blood on intravenous injection of sublethal doses. Bile was obtained aseptically by cannulation of the common duct in dogs with the cystic duct clamped off. Twenty-five samples collected over consecutive 20-minute periods after injection of 50–100 mgm/kgm. of chloroacetate were diluted 1:2 and 1:10 with broth and inoculated with 1 loopful of a 24-hour culture of *E. typhosa.* Broth, cystic bile (1:10) and hepatic bile (1:2) containing 0.05, 0.01, 0.007, 0.005, 0.003 and 0.001 per cent of added Na chloroacetate were similarly inoculated. Bacteriostasis for 48–72 hours appeared only in tubes containing 0.05 per cent added chloroacetate. Subculture to to Endo's agar after 18 hours resulted in heavy growth of *E. typhosa* in each instance Chloroacetate appears to be too weakly bacteriostatic for practical application in *E. typhosa* infections of the gallbladder. With other organisms, bacteriostasis is maximal at a low pH and presumably the undissociated acid is the effective agent. Since the pK of chloroacetic acid is $1.55.10^{-3}$, the concentration of free acid at the pH of bile is very slight with any feasible dosage.

Mechanism of the choleretic action of chloroacetate. G. A. EMERSON and JAMES L. MORRISON. *West Virginia Univ. and Emory Univ.* Carotid pressure and flow of bile were recorded in lightly barbitalized dogs prepared by cannulating the common duct and ligating the cystic duct. Hepatic bile was generally returned into the duodenum at intervals after measurement. Intravenous or intraduodenal injection of chloroacetate, 25 mg/kg., usually increased bile flow 200–300 per cent in 18 dogs. This confirms findings of Chabrol et al. (Compt. Rend. Soc. Biol. 106: 17, 1931). Chloroacetate choleresis is independent of changes in systemic blood pressure or respiration and is not due to the small amount of alkali injected. It develops slowly in contrast to the rapid, more transient effect of bile or dehydrocholate. This latency suggests mediation by some metabolite of chloroacetate. No significant choleresis was noted within 3 hours after injection of hydroxyacetate (glycolate), mercaptoacetate (thioglycolate) or aminoacetate (glycine). Chloroacetylcholine provokes a strong choleresis but the latent period is as long as with chloroacetate (45–90 min.) and this ester hydrolyses completely within a few minutes. Bromoacetate causes an effect similar to chloroacetate. There is some indication of potentiation of decholin choleresis after treatment with chloroacetate. Untreated dogs show no spontaneous variation in bile flow comparable to chloroacetate choleresis.

I. Treatment of experimentally produced staphylococcic thoracic empyema. WILLIAM E. EVANS, JR. and (by invitation) JAMES G. MCALPINE, BENEDICT SKITERALIC and E. HOWARD TONOLLA. *Univ. of Maryland, School of Medicine.* Staph. thoracic empyema was produced experimentally in approximately 100 rabbits with little or no septicemia. These animals were treated locally with drugs alone and in combination, with and without the addition of immune serum.

The most promising methods of treatment were with (1) azochloramid and sulfanilamide, (2) azochloramid and sodium tetradecylsulfate, (3) immune serum and complement, and (4) immune serum and azochloramid.

The period of treatment was limited to five days. More extensive treatment by the foregoing methods is contemplated.

Some pharmacological properties of adeninethiomethylpentose. P. L. EWING and F. SCHLENK (by invitation). *Dept. of Pharmacology and Dept. of Public Health and Preventive Medicine, Medical School, Univ. of Texas, Galveston.* Experiments were carried out to find a substitute for adenosine and adenylic acid, substances used in the treatment of certain nutritional deficiencies (R. W. Vilter, W. B. Bean and T. D. Spies. J. Lab. and Clin. Med. 27: 527, 1942). The more extensive use of these compounds is hampered by their undesirable pharmacological side-actions. In the search for a more desirable compound, the pharmacological properties of adeninethiomethylpentose (P. A. Levene and L. W. Bass, Nucleic acids, New York, Chemical Catalog Company, 1931) were studied. This compound was isolated from yeast and when purified, crystallized in long needles,

P. 210°C. Elementary analysis showed 43.94 cent C, 5.23 per cent H, 23.61 per cent N, 11.07 cent S. Formula: $C_{11}H_{15}O_3N_5S$. Calculated centages: 44.44 per cent C, 5.08 per cent H, 5 per cent N, 10.78 per cent S. This com- nd produced a fall in blood pressure in rabbits r intravenous injection. This effect was con- erably weaker than that obtained with adeno- e (about 1/10). Experiments on the isolated bit intestine showed an inhibition of the in- tinal movements by the compound—quanti- ively much weaker than that of adenosine (about 15). Its stimulating effect on the isolated inea-pig uterus was approximately the same as at of adenosine. Comparisons were also made ith muscle adenylic acid, yeast adenylic acid and zymase, each of which has pharmacological prop- ties qualitatively and quantitatively similar to ose of adenosine.

A study of combined effects of morphine with cetanilid, aminopyrine or acetophenetidin in the at. EDWIN J. FELLOWS and RAYMOND W. CUN- INGHAM. *Temple Univ. School of Medicine, Philadelphia, Pa.* The Schumacher, Goodell, rdy and Wolff method of testing analgesic agents n human subjects was suitably modified by 'Amour and Smith to permit detection of analge- sia in the rat after morphine, dilaudid, pantopon, heroin or codeine. No statements were made by these authors concerning the efficacy of the method in testing such substances as aminopyrine, acet- anilid, etc. We have been able to confirm their observations on the detection of analgesic effects in rats after administration of the opiates. We have not been able to detect analgesia by this method after acetanilid, aminopyrine or aceto- phenetidin in doses below the toxic level. Anal- getic effects, as well as a cataleptic state were obtained, however, by *intraperitoneal* administra- tion of sub-toxic doses of aminopyrine plus one-half the minimal effective dose of morphine intraperi- toneally. This sub-effective intraperitoneal dose of morphine plus either acetanilid, aminopyrine or acetophenetidin *orally* also produced analgesia detectable by the D'Amour and Smith method. These three drugs are mentioned in the order of their decreasing oral effectiveness. This apparent partial replacement of morphine by the above non- opiate analgesics in rats lends support to the evi- dence reported by Lewy which indicated that the amount of morphine given to patients with steady pain could be reduced by continuing it with other analgesics.

Assay of plasma tryptase. JOHN H. FERGUSON. *Dept. of Pharmacology, Univ. of Michigan.* In accordance with the principles for the assay of tryptases by the simple fibrinolytic method out- lined in a preliminary publication (Proc. Soc. Exper. Biol. Med. 51: 73, 1942), a convenient UNIT of 100 is defined as the proteolytic activity of 1:1000 trypsin (Fairchild's), prepared by saline dilution of 2 per cent "stock" solution (preserved in glyc- erol-borate buffer, according to Burdon, Science, 1941). The following simplified buffer (pH = 7.65) serves as solvent for fibrinogen (1:1000) and en- zyme-free thrombin: 2.5 per cent H_3BO_3 (45 parts), 0.5 per cent NaCl (45 parts), 4 per cent $Na_2B_4O_7$, $10H_2O$ (10 parts). Five cubic centimeters fibrino- gen (+ 1 cc. saline) is clotted by 3 cc. thrombin, in 30–60 seconds, and 1 cc. enzyme solution is added *exactly* 10 sec. prior to clotting, without shaking. Lysis is timed, preferably with photoelectric colorimeter: 1. series of reference standards, 100 — 1 unit; 2. unknowns. Room temperature = 25 ± 2°C.

Activation of tryptase in citrated or oxalated plasma is accomplished by shaking with 1/5 vol. $CHCl_3$ and centrifuging after 24–48 hours. En- zyme activation parallels coagulation and may be speeded up by the addition of enzyme-free throm- bin to the chloroformed plasma. Preliminary data indicate: 1. adsorption of enzyme on to *a*, Berkefeld filter; *b*, fibrin clot; 2, considerable tryptase in platelets and leucocytes, but negligible in comparison with the differences in *plasma* tryp- tase values, e.g., dog or cat 100–200 units, rabbit 1–2 units, man 40–100 units, *per cc.* Interesting applications include coagulation differences ("thromboplastic enzyme"). Prior to $CHCl_3$- activation, plasma and serum are *anti-tryptic.*

The pharmacology of some phenylethyl amines. II. Action on the intestine and heart. C. W. GEITER and A. M. LANDS (introduced by F. F. Yonkman). *Frederick Stearns and Company, and Wayne Medical College, Detroit.* The hydrochlo- rides of the compounds listed below have been investigated for their action on the isolated rabbit jejunum (Magnus method) and some of them for their action on the isolated tortoise auricle and the perfused frog heart. In the perfusion experiments all injections were made directly into the perfusion stream near the heart and the drug washed out of the tissue by the Ringer solution flowing through the organ.

Isolated segments of the rabbit jejunum were relaxed by allyl-beta-phenylethyl amine (II), in a dilution of 1:20,000; by dibutyl-beta-phenylethyl amine (IV), methyldi-beta-phenylethyl amine (V), ethyldi-beta-phenylethyl amine (VI) in 1:400,000 to 1:200,000; by propyldi-beta-phenyl- ethyl amine (VII) in 1:1,000,000 to 1:400,000. Ethyl-beta-phenylethyl amine (I), diethyl-beta- phenylethyl amine (III), and tri-beta-phenylethyl amine (VIII) were without action in dilutions of 1:10,000. However, ethyl-beta-phenylethyl amine injected intravenously into anesthetized dogs and rabbits in amounts of 0.1–0.5 mgm./kgm. caused relaxation of the intact jejunum associated with a

rise in blood pressure. The duration and intensity of the relaxation corresponded closely with the changes in blood pressure.

Compounds I, II, III and V above in 1–4 mgm. doses slow the rate of contraction of the perfused frog heart and cause some reduction in the amplitude of beat. Compound VI depresses cardiac activity; doses of 0.1–0.5 mgm. arrest all contraction in diastole. At least one half hour in Ringer solution is required to restore rhythmic contraction. Compound I in 1:20,000 causes a reduction in the amplitude with some increase in the rate of contraction of the isolated tortoise auricle. In this dilution, there is complete inhibition of the tonus waves that these preparations sometimes show. With a dilution of 1:4,000 there is a reduction in both rate and amplitude. Similar observations were made for compounds II, III, and V. Other compounds in this series were not used on the auricle.

The relative potency of U.S.P. XI and U.S.P. XII digitalis. HARRY GOLD and MCKEEN CATTELL. *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* In a large series of assays made in our laboratory by the official cat method, the potency of U.S.P. Digitalis Reference powder (1942) proved to be approximately 75 mgm. per kgm. and of U.S.P. XI powder 45 mgm. per kgm.

By definition, the U.S.P. XI Digitalis Unit is the potency of 74.5 mgm. of the XI Reference powder, and the U.S.P. XII Digitalis Unit, 100 mgm. of the XII Reference powder. Thus the XI Digitalis Unit is approximately 24 per cent stronger than the XII Unit, when the comparisons are all made by the official cat method (45:75 = 74.5:x).

By means of a method for the quantitative comparison of digitalis preparations by oral administration in man which was recently developed in this laboratory, it was found that 100 mgm. of U.S.P. XII Reference powder has the potency of approximately 75 mgm. mg. of the XI Reference powder. It follows that the U.S.P. XII Digitalis Unit has a potency practically identical with the XI Digitalis Unit when the comparisons are made directly in man.

Market preparations of U.S.P. XI Digitalis showed considerable variation in potency by the cat method, partly due to the fact that the frog method was official and partly due to other circumstances. The change from the frog to the cat method, and the change in the properties of the specimen of the Reference powder, introduced factors affecting potency which, fortunately, appear to cancel out, with the result that the Digitalis of the Twelfth Revision has substantially the same therapeutic potency as that of the preceding Pharmacopeia.

A comparison of the speed, the intensity, and the duration of action of four digitalis glycosides by intravenous injection in man. HARRY GOLD, MCKEEN CATTELL, WALTER MODELL (by invitation), NATHANIEL T. KWIT (by invitation), and MILTON L. KRAMER (by invitation). *Dept. of Pharmacology, Cornell Univ. Medical College and the Cardiac Clinics of Beth Israel Hospital and Hospital for Joint Diseases, New York City.* Animal experiments indicate that the action of digitoxin after intravenous injection develops slowly while, in the case of other glycosides, the action is more prompt. With the isolated papillary muscle, no significant differences in the latent period were observed. The latent period has not been systematically investigated in man.

We examined this problem in 21 patients with auricular fibrillation. With the patient in bed, the ventricular rate was counted at the apex three times daily for a control period of a week or longer. Counts were made at intervals of a few minutes after the drug was injected intravenously, and later at longer intervals. Counts were then made as in the control period during the next two or three weeks. The four materials tested, namely, Digitaline Nativelle, Lanatoside C, Digifoline, and Ouabain, were given in a single dose of 3 cat units (66 doses). A curve representing the development and the duration of action, averaging the results obtained in from 12 to 20 injections, was constructed for each glycoside.

The curves differ significantly. The latent period increases in the following order: Ouabain, Digifoline, Lanatoside C, Digitaline Nativelle; and the duration of action in the following order: Ouabain, Lanatoside C, Digifoline, Digitaline Nativelle. The degree of effect produced by 3 cat units is the same for Ouabain, Digifoline and Lanatoside C, but is approximately 20 per cent greater for Digitaline Nativelle.

Preliminary investigations on the pharmacology of benzimidazole. LOUIS GOODMAN, ALFRED GILMAN and NANCY HART (by invitation). *Dept. of Pharmacology, Yale Univ. School of Medicine, New Haven, Conn.* Benzimidazole HCl injected parenterally in mice, rats, cats and monkeys (200 to 300 mgm/kgm.) causes profound decrease in skeletal muscle tone and voluntary movement, lasting several hours. Consciousness is not lost. E. E. G. records reveal absence of cortical depression. Superficial and deep reflexes are diminished, corneal and pupillary reflexes are retained, postural reflexes disappear, and sensory impairment is marked, probably secondary in large measure to the motor deficit. Respiration remains adequate except with toxic doses. Preliminary emesis (cats) probably signifies medullary stimulation. Daily subeffective doses for a month cause no grossly observable behavior or tissue changes and no tolerance to effective

amounts. LD_{50} (mice) is 675 mgm/kgm., intraperitoneally. Benzimidazole is also effective orally. The spastic syndrome in a monkey with bilateral resection of cortical area 6 and caudate nucleus was improved by benzimidazole. Metrazol counteracts benzimidazole depression. Prophylactic benzimidazole decreases the incidence and severity of metrazol convulsions (mice). Benzimidazole intravenously (anesthetized cats) causes transient vasodepression and respiratory stimulation. Curariform effects on skeletal muscle are absent. Death from lethal doses is respiratory, the cardiovascular system remaining relatively unaffected.

At present benzimidazole is thought to produce its striking effects by a highly selective depressant action on the cerebrospinal axis, but the locus of this action remains to be determined. Further E. E. G. analyses, studies on congeners, and chronic toxicity experiments are in progress. Eventual clinical trial in patients with appropriate skeletal muscular and neurological syndromes is planned in view of the effect on skeletal muscle tone and the anticonvulsant property of benzimidazole. [*This research was made possible by a grant from the Fluid Research Fund of Yale University.*]

The cause of azotemia associated with massive gastrointestinal bleeding. RAYMOND GREGORY (by invitation), PAUL L. EWING and HARRY LEVINE (by invitation). *Depts. of Pharmacology and Internal Medicine, Univ. of Texas Medical School, Galveston.* Azotemia associated with gastrointestinal hemorrhage was investigated in 62 dogs by estimating the effects on blood urea nitrogen of giving dog's blood by stomach tube, of withholding water, and of lowering blood pressure by bleeding.

Blood by stomach tube may raise blood urea nitrogen to 25–30 mgm. per cent. Systolic blood pressures of 70 to 80 mm. Hg. results in rises of blood urea nitrogen to 25–40 mgm. per cent. Rise and fall of blood urea nitrogen due to blood in the stomach is faster than that due to low blood pressure. Severe anemia due to hemorrhage does not produce azotemia. Combined effects of low blood pressure and blood by stomach tube produces rapid rises of blood urea nitrogen characteristic of the latter, rises of longer duration characteristic of the former, and higher levels than one would expect from either alone.

Urea clearance is not diminished in dogs given blood by stomach tube. Falls in urea clearance occurred in every dog in which there was a significant fall in blood pressure and elevation of blood urea nitrogen. Urea clearance and blood urea nitrogen values in dogs with different water intakes indicate dehydration may contribute to azotemia associated with gastrointestinal bleeding.

Azotemia associated with gastrointestinal bleeding may be due to decreased renal function due to low blood pressure and dehydration or to absorption of digested blood. Anemia is not a factor. Absorption of digested blood from the gastrointestinal tract does not decrease renal function.

Further studies on the effectiveness of various marine oils in reducing the blood pressure of hypertensive rats. ARTHUR GROLLMAN and (by invitation) T. R. HARRISON. *Dept. of Medicine, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C.* In an earlier communication (A. Grollman, and T. R. Harrison. Proc. Soc. Exper. Biol. and Med., 1943, in press). we have presented evidence for the capacity of a variety of marine oils to reduce the blood pressure of hypertensive rats. This depressor activity was shown not to be due to the presence of vitamin A, since procedures which destroy the vitamin (ultraviolet irradiation, oxidation) tended to increase the blood pressure reducing capacity of the oils. The presence of the active principle in vitamin-A concentrates was attributed to autooxidation of some precursor other than the vitamin.

In the commercial fractionation of marine oils such as sardine body oil and dogfish or cod liver oil, slight blood pressure reducing activity is found in all fractions—those high in vitamin A, low in vitamin A and residues. It is absent from the stearin-fraction and from the glyceride fraction. The possibility of imparting activity to the latter oxidation after hydrolysis is under investigation. Morrhuic acids derived from cod liver oil are also inactive. The products obtained on their oxidation are also under investigation.

The following procedures have been found most suitable for imparting or enhancing the activity of various fractions of marine oils: oxidation with 1, hydrogen peroxide; 2, chromium trioxide, and 3, nitric acid.

The nature of the substance responsible for the observed blood-pressure-lowering effect is still unknown. It appears to be an oxidation product of some constituent (probably an unsaturated fatty acid or contaminant of the fatty acid fraction) present in various marine oils. Its relation to the principle present in mammalian kidney tissue is unknown.

Vasomotor drugs on cortical reactivity to diphenylhydantoin. P. J. HANZLIK and W. C. CUTTING and DEAN HOSKINS, HAROLD HANZLIK, E. W. BARNES and E. W. DOHERTY (by invitation). *Dept. of Pharmacology and Therapeutics, Stanford Univ. School of Medicine, San Francisco, Calif.* Conditions which might influence corticomotor excitability under diphenylhydantoin were investigated. Considerable variations in the cortical thresholds of untreated and medicated animals were found and changes of 10 per cent from

the average milliamperage were disregarded. Rabbits were used for intravenous administrations, and rats for gastric. Twelve animals were used for each drug or combination with diphenylhydantoin. All doses were per kilogram body weight, usually repeated for continued action.

The following agents used alone raised the threshold of excitability: diphenylhydantoin (2.5 mgm.), ergonovine (0.05–0.1 mgm.), ephedrine (2.5 mgm.), benzedrine (5–25 mgm., slight), calcium gluconate (1 gram, slight). The following decreased the threshold: aminophylline (10–100 mgm.), ephedrine (5 mgm., slight), papaverine (25–50 mgm.), and sodium nitrite (75 mg.). The following were ineffective: fldext. ergot (1 cc.), ergotamine (0.125 mgm.), tyramine (5 mgm.), epinephrine (0.1 mgm.), cinchophen (10 mgm.), azosulfamide (0.2 gram), quinine (40 mgm.), and parathyroid solution (0.2 cc.).

Combining the following with diphenylhydan- 'n raised the threshold for diphenylhydantoin e, chiefly by summation: ergonovine, ergota- , fldext. ergot and other ergot products. ese changes were confirmed in rats. Combinations of the following decreased the threshold for diphenylhydantoin: aminophylline, ephedrine (2.5 mgm., slight), epinephrine, tyramine, parathyroid, nitrite and papaverine. The following combinations were ineffective on diphenylhydan- oin: benzedrine, quinine, cinchophen, calcium gluconate and azosulfamide. Provisionally, it appears that a sustained generalized vasoconstriction (cerebral ischemia ?) favors the anticonvulsant efficiency of diphenylhydantoin, while vasodilatation is unfavorable.

Further observations on the antagonistic actions of N-allyl-normorphine against morphine. E. Ross Hart (introduced by C. M. Gruber). *Jefferson Medical College.* Further study has confirmed the preliminary conclusion that N-allyl-normorphine has an action similar to that of N-allyl-norcodeine in antagonizing the effects of morphine on the respiratory mechanism. Intravenous injection of 5 mgm./kgm. of the allyl derivative into rabbits will prevent or abolish the respiratory depression from 10 mgm./kgm. of morphine, depending upon the sequence of injections. When given before morphine, the allyl compound causes no stimulation of respiration and no change in the sensitivity of the respiratory center to carbon dioxide. However, when the allyl derivative is given after morphine the respiration is stimulated beyond the normal level and the respiratory center becomes more sensitive to carbon dioxide than before morphine. The hyperpnea and hypersensitivity last only a few minutes and respiration then becomes normal. Subsequent depression has not been observed up to three or four hours later at which time the experiments were discontinued because of restlessness on the part of the animal.

Observations on two cats, while not entirely conclusive, seem to indicate that N-allyl-normorphine is less stimulant in this species than morphine. Studies of other actions of this compound are in progress.

The rôle of the glossopharyngeal nerve in cardiovascular reflexes. Charles C. Herbert (introduced by Robert C. Batterman). *Dept. of Therapeutics, New York Univ. College of Medicine, and Psychiatric Division, Bellevue Hospital, New York City.* That in man the carotid sinus is innervated by the cervical sympathetic, glossopharyngeal, vagus, and hypoglossal nerves is known, but knowledge of the function of the fibers from each of these sources has been gained indirectly or only guessed, for heretofore no discreet destruction of all the fibers of one origin has been carried out and the results studied.

By section of the ninth nerve intracranially central to its ganglia, carotid sinus sensitivity was abolished ipsolaterally in a patient with bilateral sensitivity, thereby demonstrating that afferent fibers from sources other than the ninth nerve, if they exist at all, must be of little or no importance, at least as far as carotid sinus sensitivity, as we test it, is concerned. It is suggested that this operation is preferable for the treatment of carotid sinus sensitivity, as no nerve regeneration is possible. Interesting records obtained before, during, and after operation are shown.

A case of ninth nerve neuralgia initiating cardiac arrest, vasodilatation, fall in blood pressure, syncope, and generalized convulsion is presented with electrocardiographic, encephalographic, and other objective evidence of the blocking of the various components of the responsible reflex arc.

Another case of ninth nerve neuralgia associated with syncope and convulsion in a patient with carotid sinus sensitivity in addition is described. After peripheral stripping of the carotid sinus region, the sensitivity was abolished but the syncope still occurred with the ninth nerve neuralgia.

A review of the published case histories of glossopharyngeal neuralgia suggests that in several instances a similar syndrome was present, but no specific correlation among ninth nerve neuralgia, cardiac arrest, and syncope has been previously recognized.

Observations on the action of drugs in Plasmodium lophurae infections. R. I. Hewitt (by invitation) and A. P. Richardson. *Depts. of Pharmacology and Preventive Medicine Univ. of Tennessee Medical School, and the Health and Safety Dept., Tennessee Valley Authority.* The viewpoint is expressed in many published works that quinine, atabrine, or plasmochin are not directly plasmodicidal drugs, but produce their effect

indirectly in malaria. We have been particularly impressed, however, by the degenerative changes which occur in *Plasmodium lophurae* in the duck following the administration of effective drugs, not only as regards the general nature of these changes, but the specific changes produced by each drug.

When quinine, atabrine, or plasmochin are administered to ducks heavily parasitized with *P. lophurae*, all stages of the parasites show striking degenerative changes within 24 hours following the first dosage. Vacuolization, karyolysis, karyorrhexis and complete dissolution of the cytoplasm occur. When blood containing parasites from treated donors is inoculated into clean birds, using dosages comparable to control subinoculations from untreated donors, the parasitological periods are considerably delayed. Plasmochin produces the most marked effects, and subinoculations from plasmochin-treated donors produce infections of low intensity and the latent period may be delayed for as long as two weeks as compared with controls.

Degenerative changes in the parasites can also be produced *in vitro* by placing plasmochin in a test tube with heavily parasitized blood, and these changes are indistinguishable from those produced *in vivo*. We have not formed an opinion as regards the mode of action of these drugs, but whatever this mechanism may be the end result is certainly a toxic effect upon the parasites. This toxic effect is demonstrable in the changed appearance of the parasites during treatment, and the delayed infections when treated blood is used as an inoculum. [*The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Tennessee.*]

Comparison of antidotes for phenol burns of the skin. JOHN U. KEATING (by invitation) and JANET TRAVELL. *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* Some organic chemists recommend bromine in glycerin as the antidote of choice in phenol burns, since phenol is rapidly converted to tribromphenol. In rabbits and cats we compared this antidote with several others using suitable intervals after application of liquefied phenol to the unabraded skin depilated 5 days previously. Solutions of bromine in glycerin proved no more effective than glycerin alone. Furthermore, tribromphenol itself was somewhat irritant. There is therefore no justification for the above recommendation.

For removing phenol from the skin, Goodman and Gilman recommend 50 per cent alcohol or castor oil, and Sollmann, alcohol or whiskey and an oil dressing. Of the substances which we tested, 95 per cent alcohol was by far the most effective. Others ranked in order of effectiveness: (1) 25 per cent alcohol, (2) glycerin, bromine in glycerin, cod liver oil, (3) water, cottonseed oil, and (4) olive oil and castor oil. Contrary to general belief, oils differ appreciably in their antitotal value, and water and cottonseed oil have an equivalent efficiency. These conclusions were based on the degree of corrosion present 24 hours later rather than on immediate blanching; the immediate effect does not necessarily parallel the end result. This is confirmed by the widely misinterpreted experiments from Sollmann's laboratory (J. A. M. A. 46: 782, 1906) which showed blanching of the fingers exposed to liquefied phenol and treated with water, 25 per cent alcohol and 25 per cent glycerin, but no blanching with turpentine and cottonseed oil, although next day the roughening of the skin was "alike in all the fingers."

The influence of phenisopropyl amine and phenisopropyl methyl amine on work output. P. K. KNOEFEL. *Dept. of Pharmacology, Univ. of Louisville School of Medicine, Louisville, Ky.* The influence of beta-phenisopropyl-amine ("Benzedrine," "Amphetamine") and beta-phenisopropyl-methyl-amine ("Desoxyephedrine," "Pervitin") on work output was studied in seven subjects with a bicycle ergometer. The pedaling was at a constant rate of 59 revolutions per minute; the load was increased every ten minutes from the original rate of working of 560 kilogram meters per minute. At the point of inability to continue at that rate, the subject stopped and rested for ten minutes, then rode again until unable to continue. The dextrorotatory, levorotatory, and racemic forms of the compounds were used, and were alternated with lactose. Doses of 10 or 20 mgm. of the sulfates of the compounds were given two hours before working. The greatest augmentation of work output in any subject was from an average of 25,320 kgm. m. with lactose to 40,745 kgm. m. after 10 mgm. *dl* phenisopropyl-methyl-amine. Four other subjects gave smaller increases in work output, two were not influenced by the doses given. With each compound, the dextro isomer was more active than the levo isomer. Twenty mgm. of the racemic compound was more active than 10 mgm. of the dextro form. Comparisons of the phenisopropyl-amine and the phenisopropyl-methyl-amine were obtained in five subjects. The methyl-amine was the more active in three of these, the amine the more active in two. An increase in arterial pressure commonly resulted from the compounds, and was uniformly greater with the phenisopropyl-amine. [*These experiments were done in the Department of Physiology, University of Wisconsin School of Medicine.*]

The vasomotor reversal in yohimbine-treated dogs. THEODORE KOPPANYI, CHARLES R. LINEGAR and ROBERT P. HERWICK. *Dept. of Pharma-*

cology and Materia Medica, Georgetown Univ., School of Medicine. Yohimbine and its derivatives are usually considered sympatholytic and adrenolytic drugs, pharmacologically allied with ergotoxine. Experiments performed in dogs under various anesthetics yielded the following results:

1. Yohimbine does not have an ergotamine-like initial pressor effect but always produces a considerable fall in blood pressure. This fall is minimized by injecting the drug intramuscularly.

2. Yohimbine (aphrodine) hydrochloride, in doses of 1.0 mgm. per kilogram or more given by vein of 3.0 mgm. or more given by muscle, produces a vasomotor reversal to epinephrine irrespective of the anesthetic agent. It is, unlike the ergot alkaloids, fully effective under barbiturate narcosis. The larger the dose of epinephrine the greater the fall in blood pressure except when excessive doses are employed.

3. In animals, showing complete vasomotor reversal to epinephrine, electrical stimulation of the lumbar sympathetic chain resulted in blood pressure rises comparable to those seen before yohimbine administration. These vasopressor responses often followed by appreciable falls in blood pressure which could be prevented by clamping both adrenal veins.

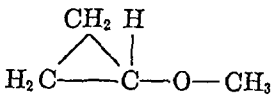
4. The effect of adrenin mobilized by nerve stimulation or by adrenal massage is reversed by yohimbine. Nor-epinephrine effects are not reversed.

5. Atropine yielded variable results; in some cases it abolished or diminished the vasomotor reversals and in others it left them unchanged.

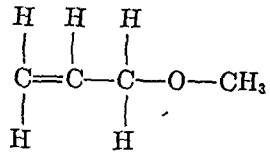
Yohimbine did not interfere with the pressor effects of nicotine and of large doses of acetylcholine (in atropinized animals).

It is concluded that the vasomotor reversal seen after yohimbinization cannot be adequately explained on the basis of sympathetic paralysis.

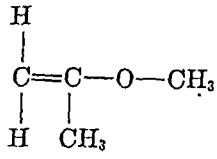
The anesthetic properties of isopropenyl methyl ether. JOHN C. KRANTZ, JR., C. JELLEFF CARR, WILLIAM E. EVANS, JR. and by invitation, SYLVAN E. FORMAN. *Dept. of Pharmacology, School of Medicine, Univ. of Maryland.* In a former communication the authors reported their studies on the anesthetic properties of cyclopropyl methyl ether (Cyprome Ether) and its isomer, allyl methyl ether. The former gave promise in its pharmacological investigations and has been used successfully in man. The latter was irritatingand hepatotoxic to several species of laboratory animals and was hence not used clinically. In the study of the isomers of cyprome ether, the authors prepared isopropenyl methyl ether. This compound has been called isoprome ether. Structural relationships are apparent from the following formulas.



Cyprome ether



Allyl Methyl Ether



Isoprome Ether

It is a volatile colorless liquid with an ethereal, characteristic odor and boils at 35°C.

Its anesthetic index appears to be 3 times greater than ethyl ether and its potency is approximately equal to that of cyprome ether. In many species of laboratory animals it is an excellent anesthetic giving rise to complete relaxation of the abdominal musculature. Other studies are in progress on animals and on man.

The action of some "heart stimulants" on the contraction of isolated mammalian cardiac muscle. STEPHEN KROP (introduced by McKeen Cattell). *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* The action of camphor, pentamethylene tetrazol ("Metrazol", "Cardiazol", nikethamide (diethylamide of pyridine β-carboxylic acid) ("Coramine"), and barium chloride was studied on the force of contraction of isolated mammalian cardiac muscle. The heart muscle preparation used was the papillary muscle of the cat's right ventricle, "driven" rhythmically at a constant rate by electrical stimulation and under constant initial tension in Locke's solution at 38°C. The isometric response was recorded photographically at intervals. When the "systolic" tension became steady, the above drugs in suitable quantity were added to the Locke's solution.

Camphor did not increase the "systolic" force at any concentration used; in concentrations of 1,25,000 it caused a reduction of the "systolic" force. The toxic effects of higher concentrations were a marked reduction in contractile force and, ultimately, inexcitability. Pentamethylene tetrazol likewise did not increase the "systolic" tension even in concentrations as high as 1:1,000; it is nontoxic at concentrations as high as 1:1,000. Nikethamide also was ineffective, and caused depression at 1:5,000 or higher concentrations. Barium chloride was found toxic in 1:5,000 and higher concentrations, and has no "digitalis-like action."

It is concluded that the above drugs are incap-

able of augmenting the force of failing mammalian cardiac muscle in concentrations expected in the blood stream of man following therapeutic doses. Consequently any alterations in cardiac function which might occur after these drugs in the intact mammal or in the isolated heart or heart-lung preparation are presumably secondary to changes in heart rate, coronary flow, or venous return to the heart.

The pharmacology of some phenylethyl amines. I. Vasopressor, nydriatic action and toxicity. A. M. LANDS and C. W. GEITER (introduced by F. F. Yonkman). *Frederick Stearns and Company, and Wayne Medical College, Detroit.* In this investigation the hydrochlorides of the following were used: ethyl-beta-phenylethyl amine (I), allyl-beta-phenylethyl amine (II), diethyl-beta-phenylethyl amine (III), dibutyl-beta-phenylethyl amine (IV), methyldi-beta-phenylethyl amine (V), ethyldi-beta-phenylethyl amine (VI), propyldi-beta-phenylethyl amine (VII) and tri-beta-phenylethyl amine (VIII). Compound I, 0.05 mgm./kgm., injected intravenously into dogs anesthetized with nembutal, produced a rise in carotid pressure. Doses of 0.5 mgm./kgm. induced rises of 30–80 mm. Hg lasting 10–20 minutes. Doses of 0.5–2 mgm./kgm. produce an initial but transient fall followed by the sustained rise in pressure. These responses are not potentiated by cocaine. Compounds II, VII and VIII were without effect on blood pressure, III and VI caused a transient fall and V usually caused a fall although in a few instances the fall was followed by a slight rise. Compound IV caused a transient fall, followed again by a slow reduction in blood pressure. Doses as large as 0.5 mgm./kgm. sometimes caused death.

In the unanesthetized dog, the subcutaneous injection of 0.5–1 mgm./kgm. of compound I gave a rise in systolic blood pressure of 15–25 mm. Hg within 20–40 minutes and lasting 60–80 minutes. A bradycardia of 15 to 30 beats/minute was observed at the peak of the pressure. The heart rate returned to normal somewhat more slowly than did the blood pressure. A 2 per cent solution of compound I instilled into the human conjunctival sac caused a maximum degree of mydriasis within 2 hours with some pupillary dilatation for over 4 hours. Intravenous injection of 20–30 mgm./kgm. into unanesthetized albino rabbits caused moderate mydriasis, lasting about 30 minutes.

Compound I has a low toxicity. Subcutaneous doses of 300–800 mgm./kgm. caused only an occasional death. Intravenous injections of 75 mgm./kgm. as a 2 per cent solution into albino rabbits were tolerated.

The action of antispasmodic drugs on uterine motility. G. LEHMANN. *Dept. of Pharmacology, Univ. of Louisville School of Medicine, Louisville, Ky.* There is an apparent contradiction between the clinical usefulness of antispasmodic drugs like syntropan in dysmenorrhea and their action on uterine motility in experimental animals. For this reason the action of such drugs has been studied on isolated strips of human uteri. Syntropan and other tropic acid derivatives produced either contraction or had no effect while a number of other drugs caused relaxation. These were substances which were able to relax spasm of the intestine, produced by histamine. Thus only compounds with a marked histamine-antagonizing action induced relaxation of the myometrium, whereas substances which lack this property, as atropine and syntropan had either no or astimulating action. The acetylcholine-antagonizing action of these compounds is apparently not concerned with the relaxing effect of antispasmodic agents. Somewhat similar results were obtained from experiments on decerebrate cats and anesthetized rabbits, both in "vivo" and in "vitro."

This suggests that the pain-relieving action of syntropan and similar drugs is hot due to relaxation of the corpus uteri.

The influence of the potassium content of the environment on the action of the cardiac glycosides on the isolated heart. ROBERT A. LEHMAN and GEORGE PAFF (by invitation). *Dept. of Therapeutics, New York Univ. College of Medicine and the Dept. of Anatomy, Long Island College of Medicine.* The qualitative effect of a number of cardiac glycosides on the isolated embryonic chick heart has been previously described and the relationship between time and concentration has been explored with respect to the initiation of atrio-ventricular block. Thus it was found that the logarithm of the concentration of the glycoside is a linear function of the logarithm of the time necessary for the appearance of block. Using the same technique, a family of log time-log concentration curves was determined for the same glycoside at concentrations of potassium in the Tyrode solution bathing the heart ranging from 1.5 to 11.0 millimols per liter. From each of these curves there was computed by interpolation a concentration of the drug with its standard error which would produce atrio-ventricular block at one arbitrarily selected time. It immediately appeared that the glycoside concentrations so obtained were directly proportional to the potassium concentration of the medium. The same relationship was found to hold for each member of the family, lanatoside A-digitoxin (Merck)-digitoxigenin, which are representative of the genuine glycoside, progenin, and genin types respectively. It should be pointed out that the potassium concentrations used in these experiments were within the range which permit the embryonic heart to function normally. It was further found that at potassium concentrations

below one millimol per liter a typical atrio-ventricular block will appear in the absence of a cardiac glycoside. It is generally conceded that the glycosides in toxic amounts will cause a loss of potassium from the isolated or intact mammalian heart. Hence the data suggested that a high potassium concentration in the external environment decreases the concentration of differential within and without the muscle cells with the result that proportionately more glycoside is necessary to produce block within the same time.

The antispasmodic action of some para-xenyl acetic acid esters. J. R. LEWIS, A. M. LANDS and C. W. GEITER (introduced by F. F. Yonkman). *Frederick Stearns and Company, and Wayne Medical College, Detroit.* The antispasmodic action of the hydrochlorides of several derivatives of the biphenyl compounds, b-diethylaminoethyl-p-xenyl acetate, b-piperidinoethyl-p-xenyl acetate, y-diethylaminopropyl-p-xenyl acetate and y-piperidinopropyl-p-xenyl acetate, has been determined on the isolated rabbit jejunum according to the technique of Magnus. Compounds with a methyl, ethyl, propyl, phenyl or cyclohexyl substitution on the acetate radical were tried for all the above esters except the last, in which case only the methyl and phenyl substitutions were available. In all instances, the methyl derivatives were the most active. Thus b-diethylaminoethyl-p-xenyl acetate HCl relaxes the unstimulated jejunal segment in 1:100,000–1:200,000 whereas b-diethylaminoethyl-methyl-p-xenyl acetate relaxes in 1:1,000,000–1:2,000,000; b-piperidinoethyl-p-xenyl acetate relaxes in 1:200,000–1:400,000 whereas b-piperidinoethyl-methyl-p-xenyl acetate will relax in 1:2,000,000–1:4,000,000; y-diethylaminopropyl-p-xenyl acetate relaxes in 1:40,000 whereas y-diethylaminopropyl-methyl-p-xenyl acetate relaxes in 1:1,000,000–1:2,000,000. Compound y-piperidinopropyl-methyl-p-xenyl acetate relaxes in 1:500,000–1:1,000.000. Increase in the size of the substituted group to ethyl, propyl, phenyl, or cyclohexyl, resulted in a reduction in antispasmodic activity from that of the methyl compound.

Intravenous injection of b-piperidinoethyl-methyl-p-xenyl acetate were made into anesthetized dogs and rabbits and recordings made of the motility of the intact jejunum. Moderate relaxation was obtained in the rabbit with 0.05–0.1 mgm./kgm. and in the dog with 0.5 mgm./kgm., lasting for about 15 minutes. Intravenous doses of 1.0 mgm./kgm. had no effect on the carotid blood pressure of dogs. The p-xenyl acetates are irritating to the rabbit conjunctiva; with resulting hyperemia and edema and in some instances corneal opacity. The toxicity of the most active compound, b-piperidinoethyl-methyl-p-xenyl acetate, was determined in albino mice by intraperitoneal injection. A dose of 150 mgm./kgm. killed 13 out of 25 mice, most of the deaths occurring within the first few minutes. In general, toxic manifestations were those of central stimulation.

The place of gelsemine in autonomic pharmacology. CHARLES R. LINEGAR, THEODORE KOPPANYI and FRANK A. BARTIMO (by invitation). *Dept. of Pharmacology and Materia Medica, Georgetown Univ., School of Medicine.* Piperidine and its allies, coniine and sparteine, depress both parasympathetic and sympathetic ganglia as shown by the abolition of the cardiac vagus effect and the pressor response to nicotine. They do not interfere with the vasodepressor effect of acetylcholine; the pressor effect of epinephrine is potentiated rather than abolished following their administration.

Since gelsemine is considered a close ally of coniine, it was deemed advisable to reinvestigate its pharmacological action. The results obtained in dogs established that there is no similarity between gelsemine and the piperidine allies.

1. Gelsemine (Gelseminine hydrochloride—Merck) in doses of 0.1 to 3.0 mgm. per kgm. injected intravenously produces a sharp fall and not a rise in blood pressure. On intramuscular administration it has no effect on blood pressure. The magnitude of vasodepression diminishes on repeated administration until no effect is obtained. Larger initial doses produce acute tolerance more rapidly. Intramuscular injection of large doses also protects against vasodilation from intravenous doses of gelsemine. This tachyphylaxis is, therefore, similar to that seen after morphine administration; intravenous doses of morphine produce only slight falls in blood pressure in animals treated with gelsemine, thus showing that gelsemine protects against morphine.

2. Since gelsemine abolishes the effect of the electrical stimulation of the cardiac vagus and also of intravehous acetylcholine injections, its point of action is probably not located in the parasympathetic ganglia.

3. Gelsemine does not abolish the pressor effect of nicotine, on the contrary, in some cases these pressor effects appear potentiated.

4. Gelsemine does not enhance the pressor effect of epinephrine.

Intravenous ("slow drop") toxicity of sobisminol in experimental syphilis. F. P. LUDUEÑA. *Dept. of Pharmacology and Therapeutics, Stanford Univ. School of Medicine, San Francisco, Calif.* Sobisminol solution injected intravenously by a slow "drip method" was found to be about once as again as toxic in syphilitic rabbits as in the normal. The local lesions and infectious organisms were not affected because an adequate antisyphilitic dose of bismuth could not be administered due

to lack of tolerance for the metal intravenously. Confined normal and syphilitic rabbits showed definite reductions in plasma ascorbic acid, but the prolonged administration of large doses of ascorbic acid did not increase the tolerance of sobisminol intravenously, nor did this vitamin have a demonstrable antidotal action. Therefore, there was no demonstrable relationship of a hypovitaminosis of C and an intolerance of bismuth as has been reported clinically for the arsenicals and some other heavy metals. The intravenous intolerance and antisyphilitic inefficiency confirm the long suspected undesirability of using bismuth intravenously in treating syphilis.

D-tubocurarine and quinine methochloride. A. R. McINTYRE and R. E. KING (by invitation). *Dept. of Physiology and Pharmacology, Univ. of Nebraska College of Medicine, Omaha.* Although both the active alkaloid of *Chondodendron Tomentosum* (d-tubocurarine) and quinine methochloride block motornerve impulses at the nerve-muscle junction, we have found many pharmacological differences between them. Quinine methochloride inhibits dog-serum cholinesterase, d-tubocurarine does not. When quinine methochloride is injected intra-arterially into a dog anesthetized with sodium barbital, paralysis of the myoneural structures supplied by the injected artery is not abolished by either acetylcholine or physostigmine. Acetylcholine and physostigmine both antagonize d-tubocurarine paralysis. Asphyxia augments the paralytic action of quinine methochloride but with tubocurarine asphyxia appears to render the myoneural junction somewhat more resistant to paralysis. The duration of a minimal paralytic dose (M.P.D.) of quinine methochloride is approximately only one fourth the duration of a M.P.D. of d-tubocurarine. Subparalytic doses of quinine methochloride at first slightly augment the muscle-response to single spike shocks applied to the nerve, there is no augmentation with d-tubocurarine. Intravenously injected, quinine methochloride causes a sharp fall in blood pressure and an initial stimulation of respiration. D-tubocurarine causes no change in blood-pressure and no initial stimulation of respiration. The differences of the two substances upon the blood-pressure and the respiration are possibly explained by their difference in action upon serum cholinesterase.

Pulmonary and systemic blood pressure changes produced by intravenous injections of neoarsphenamine. DAVID MARSH (by invitation) and R. A. WOODBURY. *Dept. of Physiology and Pharmacology, Univ. of Georgia School of Medicine, Augusta.* Simultaneous arterial and venous pressures of the systemic and pulmonary circulations were determined by sounds in the right and left ventricles. Intact rabbits, cats and dogs (with and without anesthesia) receiving 100 mgm kgm. of neoarsphenamine showed the typical fall in systemic arterial pressure (SAP) and rise in pulmonary arterial pressure (PAP). The pulmonary venous pressure (PVP) was not elevated· this proves that the elevated PAP is not dependent upon left heart inadequacy. An increased pulmonary resistance is responsible since the pulmonary gradient (PAP minus PVP) became greater.

Pulmonary vasoconstriction, multiple emboli and injury to the pulmonary vascular endothelium have been suggested as the cause for increased pulmonary resistance. Vasoconstriction may contribute little, since vasomotor drugs in dogs, even in large doses, fail to produce significant increase in pulmonary resistance. Multiple emboli do not play a necessary role because injection of the drug in sufficient dose into a portal branch produced a delayed rise in PAP of about the same extent as half the dose into a systemic vein. Direct damage to the lungs was evidenced by the frequent finding of severe pulmonary edema in dogs and rabbits but not cats, regardless of the route of administration or of the elevation of PAP.

Epinephrine does not antagonize the rise in pulmonary pressure since cardiac inadequacy was not present. Atropinization does not prevent the rise in pulmonary pressure. [*This work was aided by a grant from the American Medical Association.*]

The optimal dose of mercurial diuretics. WALTER MODELL (introduced by Harry Gold). *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* The effects of varying doses and different modes of administration of mercurial diuretics were studied in 37 ambulatory patients with congestive heart failure. These patients all required diuretics to maintain a resonable state of comfort. The effects of the diuretics were determined by the loss of weight produced in approximately 15 hours. With periodic doses it was possible to maintain an equilibrium between the diuresis produced by the mercurial and the edema which accumulated in the period between injections. Thus the weekly weight curve was flat and the diuretics were given to patients in essentially the same state on each occasion.

Alternate injections of varying doses were made in the same patients and compared; each subject therefore acted as his own control. A sufficient number of injections were made to give statistically valid data.

These results indicate that the relative effectiveness of small doses of mercurial diuretics is greater than that of large doses. For example, the total diuresis produced by a 2 cc. intravenous injection is on the average only 25 per cent greater than that produced by a 1 cc. dose. The use of ammonium chloride increased the effectiveness of both 1 and 2 cc. doses by about 15 per cent. The administration of two 1 cc. doses a week, separated by an

interval of 3 or 4 days, produced 20 per cent greater total weight loss than a single 2 cc. injection weekly, and also maintained the patient in a state of greater comfort. It was also found that intravenous and intramuscular injections of the same dose produced the same amount of diuresis.

Effects of d-, l- and r-amphetamine sulfate on the oxygen consumption of morphinized dogs. JAMES L. MORRISON (by invitation) and BENEDICT E. ABREU. *Depts. of Pharmacology and Physiology and Pharmacology, Emory Univ. School of Medicine, Atlanta, and Univ. of Georgia School of Medicine, Augusta.* The oxygen uptake of brains of dogs depressed by morphine has been shown to be increased by r-amphetamine (Am. J. Physiol. **133:** P314, 1941). Other studies (U. C. Publ. Pharmacol. **2:** 99, 1942) indicate that the oxygen consumption of morphinized rats is increased by r-amphetamine. Since the activity of the three isomers of amphetamine varieties, d-amphetamine usually being the most active (Proc. Soc. Exper. Biol. and Med. **42:** 206, 1939), their influence upon the oxygen consumption of morphinized dogs was investigated.

Oxygen consumption determinations were done in duplicate by means of the Sanborn Motor-Grafic Metabolor on 4 dogs which had received morphine sulfate 10 mgm./kgm., subcutaneously, 50 minutes previously. These two values were used as controls. Each animal then received 0.5 mgm./kgm. dosages intravenously of either r-amphetamine sulfate, d-amphetamine sulfate or l-amphetamine sulfate after which duplicate determinations of oxygen consumption were made. Animals were allowed to recover for a period of 3–4 days following the administration of morphine and one of the ·[illegible]tamines. The oxygen consumption was increased from the basal morphine level by r-amphetamine 13 per cent (10–14), by d-amphetamine 22 per cent (14–34) and by l-amphetamine 15 per cent (4–30).

Only the change produced by d-amphetamine has as yet been shown to be significantly different from that resulting from l- or r-amphetamine administration. [*This work was aided by a grant from the American Medical Association.*]

The complete inhibition of the hypoglycemic action of insulin during ether anesthesia. S. A. PEOPLES. *Dept. of Physiology and Pharmacology, Univ. of Alabama School of Medicine, University.* Dogs were anesthetized with ether, using a closed system in order to maintain a constant level of anesthesia for 2 hours. In series A 4 units per kilo of insulin were given subcutaneously one minute before the anesthesia was begun. In series B no insulin was given. Blood samples were taken every 30 minutes during and for 3 hours after the anesthesia and analyzed for glucose, CO_2 combining power and lactic acid.

The blood sugar curves during anesthesia were essentially the same in both A and B, rising quickly to 175–225 mgm. per cent and levelling off there. During recovery in B there was a gradual return to normal values over a period of 2–3 hours, but in A there was a rapid fall to convulsive levels in 1–1½ hours. The fall in CO_2 combining power and the proportional rise in lactic acid during anesthesia were the same in both A and B, but during recovery their return to normal was delayed.

Ether apparently has the property of completely inhibiting the hypoglycemic action of insulin. That this is an inhibition and not destruction or increased elimination is shown by the fact that dogs regularly developed convulsions 1–1½ hours after anesthesia or 3–3½ hours after the insulin was given.

Trypanocidal activity and arsenic content of rat blood following intravenous administration of mapharsen. LAWRENCE PETERS (by invitation) and HAROLD N. WRIGHT. *Univ. of Minnesota Medical School.* The relationship of the arsenic content of rat blood following the intravenous administration of maximum tolerated doses of mapharsen to the degree of trypanocidal activity of the blood was determined by comparing the trypanocidal activity in vitro of successive dilutions of blood removed from injected rats at varying time intervals against the direct in vitro trypanocidal activity of mapharsen using the same dilution medium and trypanosome inoculum. Cultures were examined microscopically after eighteen hours incubation at 37°C and checked by intraperitoneal inoculation into rats or mice.

The trypanocidal period showed three phases. During the first hour the arsenic content and trypanocidal activity of the blood declined parallel to one another, the trypanocidal activity of the blood being equal to that which could be expected on the basis of its arsenic content, the percentage of arsenic possessing trypanocidal activity being 100 per cent after two and one-half minutes. 98 per cent after fifteen minutes, and 91 per cent after one hour. From the second to the eighth hour, the trypanocidal activity declined much more rapidly than the arsenic level, only 15 per cent being trypanocidal after four hours and 4.5 per cent after eight hours. Between twelve and forty-eight hours a secondary rise in blood arsenic occurred, but the trypanocidal activity continued to decline, only 1 per cent being trypanocidally active after twelve and eighteen hours, 0.5 per cent after twenty-four hours, and the blood completely losing its trypanocidal properties after thirty-six hours, although the arsenic concentration was 200 times the minimum concentration required for trypanocidally active arsenic.

The effect of growth-factor upon the body weights of starving or underfed rats. LEO

POMERANTZ (by invitation) and MICHAEL G. MULINOS. *Dept. of Pharmacology, College of Physicians and Surgeons, Columbia Univ., New York City.* The loss in body weight occurring during complete starvation or underfeeding can be influenced by anterior pituitary extracts. Experimentally underfed rats with a constant low body weight have been made to gain weight when injected with growth-factor, (Squibb Anterior Pituitary Extract), despite continued underfeeding. When injections of growth-factor were begun simultaneously with the beginning of a starvation or underfeeding period, rats lost less in weight than did their saline injected littermate controls. Cessation of injections of growth-factor resulted in a sudden drop in body weight towards the level of the controls.

When rats were refed after a prolonged period of under-nutrition (6 to 12 mos.) they gained rapidly in body weight. However, this precipitous rise in weight could be further augmented by injections of growth-factor. The augmentation was not as noticeable during the initial period of weight rise (when the rate of gain was very marked) as it was when the slope of the body weight curve began to plateau. The greater gain in body weight of the refed growth-factor injected rats, over that of the refed controls was not dependent upon an increased food and water intake, because the increased gain occurred on amounts of food and water about equal in the two groups.

In previous work (J. Nutrition 19: 493, 1940) it was shown that inanition depressed the adrenotropic and gonadotropic activities of the hypophysis. It is suggested that the depression of the hypophysis results in a diminution of the growth-factor activity of the gland as well.

On the supposed synergism of morphine and strychnine. E. L. PORTER and J. C. LOCKHART (introduced by C. D. Leake). *Dept. of Physiology, Medical School, Univ. of Texas, Galveston.* It has been supposed that morphine and strychnine act synergistically on the nervous system of the organism, the spinal cord being primarily involved. Such synergism would not be expected in view of the general depressant action of morphine. We have tested the matter on the spinal cat where the spinal cord is the only surviving portion of the nervous system. Using a small flexor muscle of the hind leg and stimulating a pain nerve through a special electrode, we have established a base of small contractions near the threshold. Upon giving small doses of strychnine intravenously, the reflex reaction is increased as shown by a greater height of the record on the drum. If now a solution of morphine sulphate is injected intravenously the reflex is diminished and the contraction height lowered. By using sufficiently small doses of these drugs, this reaction may be repeated many times on the same animal, indicating a strict antagonism between the two drugs under the conditions of our experiment. This suggests that the supposed antagonism between morphine and strychnine is a therapeutic one and not basic, and that its site is not the cord but some higher portion of the nervous system.

Phthalylsulfathiazole, a new bacteriostatic agent. EDGAR J. POTH and CHARLES A. ROSS (introduced by C. D. Leake). *Laby. of Experimental Surgery, Univ. of Texas Medical School, Galveston.* An extension of the studies on acylated sulfonamides as intestinal antiseptics, which produced the compound succinylsulfathiazole, has uncovered another effective derivative of this series of drugs, phthalylsulfathiazole. This compound, like succinylsulfathiazole, is sparingly absorbed from the gastrointestinal tract, maintains low concentrations in the blood, and is rapidly excreted in the urine. Phthalylsulfathiazole has 2 to 4 times the bacteriostatic activity of succinylsulfathiazole in the bowel, but does not appear to alter so greatly the consistency of stools. Microorganisms in the stools are usually greatly decreased in 24 hours by phthalylsulfathiazole, and coliforms are ordinarily reduced to less than 1000 per gram of wet feces within three days.

The oral administration of phthalylsulfathiazole at 4 hour intervals has not caused any toxic symptoms in dog or man. On clinical trial, it seems to be effective in the presence of a persistent watery diarrhea. It has about twice the bacteriostatic activity in humans as in dogs.

The concentration of sulfathiazole in the blood of a dog receiving 0.5 gram of phthalylsulfathiazole per kilo of body weight daily varies from 0.5 to 2.5 mgm. per cent free, and from 0.5 to 3.5 mgm. per cent total, while for man on an adequate therapeutic dose of 0.125 gram per kilo of body weight the concentration varies from 0.10 to 1.0 mgm. per cent free and 0.3 to 2.0 mgm. per cent total.

Further studies on the effect of sodium bisulphite upon the toxicity of drugs. R. K. RICHARDS (introduced by E. M. K. Geiling). *Abbott Laboratories, North Chicago, Ill.* In a previous communication (Federation Proc. 1: no. 1, 71, 1942) we reported a remarkable increase of the toxicity of epinephrine by the addition of as little as 0.1 to 0.2 per cent $NaHSO_3$. This was observed in rats and other species by i.m. and subcu. injection. The following represents studies regarding the influence of $NaHSO_3$ upon the toxicity of a few other drugs.

Methylaminoethanolphenol (Neo Synephrin) was found to have an L.D. 50 of approximately 40 mgm./kgm. i.m. in rats. Addition of 0.2 per cent $NaHSO_3$ decreased the L.D. 50 to 22 mgm./kgm. The toxicity of ephedrine remained uninfluenced by $NaHSO_3$. The convulsive dose of procaine

i.m. in rats was lowered from approximately 1000 to 175 mgm./kgm. and the L.D. 50 from 1600 to 400 mgm./kgm. by the presence of 0.1 per cent $NaHSO_3$. Other acid buffers, as sodium acid phosphate, or reducing agents, as sodium hypophosphite, failed to act like $NaHSO_3$. The increase in toxicity with procaine could not be observed with certainty in rabbits or dogs.

These results are interpreted as an indication that an increase of toxicity by the presence of $NaHSO_3$ occurs only with such drugs which are rapidly detoxified in the body. The presence of $NaHSO_3$ appears to greatly enhance the speed of absorption, probably by a local action upon the capillaries. It is at least possible that this represents to a certain degree a specific effect, since other compounds with similar physical—chemical properties do not produce corresponding increases in toxicity.

Experimental studies on the nourishment of the left ventricle by the lumenal (Thebesial) vessels. JOSEPH T. ROBERTS (introduced by C. D. Leake). *Depts. of Anatomy and Medicine, Univ. of Texas Medical School, Galveston.* In six experiments on dog hearts beating in situ, Chicago Blue dye (2 per cent) was injected with pressures of 120 mm. of mercury into the left ventricle through a cannula in the left atrium. This was done immediately after having ligated simultaneously both main ronary arteries, the aorta, pulmonary artery d veins, and venae cavae. In each experiment ıe dye appeared immediately in the peripheral ends of the coronary arteries and veins, usually first near the apex of the left ventricle. The dye flowed toward the base of the heart in filling the coronary arteries and veins.

In a dead heart both main coronary arteries were ligated and dye was injected with a pressure of 35 mm. of mercury into the left ventricular cavity by way of a cannula introduced through the aorta. At once dye appeared in numerous spots around the apical ends of the smaller coronary arteries and veins on the surface of the heart. From the smaller vessels the dye flowed into the larger ones.

It is believed that the lumenal (Thebesian) vessels can conduct blood from the left ventricle into the myocardium under circumstances where the pressure in the chamber is greater than that in the coronary vessels.

Nourishment of the myocardium by way of the coronary veins. JOSEPH T. ROBERTS, R. S. BROWNE and GERTRUDE ROBERTS (introduced by C. D. Leake). *Depts. of Anatomy and Medicine, Univ. of Texas Medical School, Galveston.* In 14 dogs with hearts in situ, additional arterial blood was brought to the myocardium by a glass cannula connecting the coronary sinus with the brachiocephalic, subclavian, or innominate artery. The coronary veins became distended, pulsatile, and arterial in color. After reversal of flow in the coronary veins, the anterior descending coronary artery was ligated in two experiments, the anterior descending and left circumflex arteries in one experiment, the anterior descending and right coronary arteries in one, and the right coronary artery in one. The hearts continued to beat regularly and forcefully for periods ranging from 10 minutes to 26 hours.

In 10 dogs with normal rhythm or immediately after stoppage of the heart or ventricular fibrillation, Chicago Blue dye (2 per cent) was injected into the coronary sinus with pressure of 100 mm of mercury. Sections of the myocardium revealed a complete injection of the capillaries.

The small valve, sometimes found at the left end of the coronary sinus, was present and capable of preventing reversal of flow in one other heart.

These preliminary experiments suggest that an ischemic myocardium may be revascularized by anastamosis of a large artery with the coronary sinus and coronary veins.

Effects of devascularizing the sciatic nerve. JOSEPH T. ROBERTS, WALTER H. JARVIS and JULIAN KEY (introduced by C. D. Leake). *Depts. of Anatomy and Medicine, Univ. of Texas Medical School, Galveston.* The concept that peripheral neuropathy (neuritis) may be due to ischemia of peripheral nerves was tested experimentally in 23 dogs by various procedures: ligating the nutrient arteries of the sciatic nerve, gently stripping away its perineurium and its blood vessels, crushing or stretching the nerve, placing bands around the nerve, compressing the limb with a tourniquet, or producing arterial embolism with air or lycopodium spores. After injection of 2 per cent Chicago Blue into the aorta the nerves were examined grossly, microscopically and after clearing. The ischemic segment showed little or no injection. The normal contralateral nerve had a rich plexus of arterioles, venules and capillaries in the perineurium, anastomosing longitudinally; inside the nerve a rich anastomosis of capillaries was found.

In 26 dogs chronic ischemia was produced by performing surgically the same procedures as above, except that graphite was used to produce embolism. Gradual compression was produced in 6 growing kittens by growth with a restricting band on the nerve. During survival of from 5 days to 4 months the observed effects included: paralysis, loss of tone and atrophy of the muscles, altered reflexes, impaired sensation, trophic ulcers and degeneration of nerve fibers (especially the large myelinated fibers). In control operations where the nerve was exposed in the same manner but without injury to the vasa nervorum, no abnormalities were observed.

Drainage of myocardium by cardial lumenal (thebesian) vessels of the left ventricle. Jo-

SEPH T. ROBERTS, FRED D. SPENCER, JR. and R. S. BROWNE (introduced by C. D. Leake). *Depts. of Anatomy and Medicine, Univ. of Texas Medical School, Galveston.* In 38 dogs with hearts beating in situ, Chicago Blue (2 per cent) was injected into the cannulated anterior descending coronary artery with pressure just below the systemic arterial blood pressure. "Liquaemin" (Roche-Organon, Inc.) prevented coagulation. Dye appeared in the aortic blood immediately or within 3 to 10 seconds. Possibility of the dye reaching the aorta through other routes than the lumenal (Thebesian) vessels was excluded by the following methods: (1) ligating both main coronary arteries at the instant of injection; (2) a bottle-and-bag shunting device in the pulmonary artery, or ligating the pulmonary vessels at the instant of injection; (3) absence of dye in the incised lung during the experiment; and/or (4) appearance of dye in aortic blood as tiny spurts instead of being mixed uniformly with the blood. The shunting device consisted of a cannula in the proximal incised pulmonary artery, leading to a collapsed rubber bag contained in a bottle which was filled with blood or Locke-Rosenheim solution; the bottle was connected to the distal pulmonary artery. Dye reaching the right ventricle was caught in the rubber bag.

By way of the lumenal (Thebesian) vessels, blood can be drained from the myocardium into the cavity of the left ventricle in the heart beating in situ. This study did not demonstrate the phase or phases of the heart's cycle during which such flow occurs.

Distribution and retention of arsphenamines in relation to physical properties. F. B. RODMAN (by invitation) and HAROLD N. WRIGHT. *Univ. of Minnesota and Univ. of Alberta, Canada, Medical School.* The distribution to and retention in eleven tissues or organs has been determined for arsphenamine, neoarsphenamine, and the separated crystalloid and colloid fractions of both drugs for periods from 30 minutes to 14 days after intravenous administration. Analyses at early time intervals accounted for all the administered drug.

In the case of arsphenamine 18 per cent of the administered drug remained in the blood half an hour after injection, but had disappeared after twenty-four hours; the crystalloid fraction showed 19 per cent in the blood after half an hour, and 6–8 per cent at all other intervals to fourteen days; the colloid fraction was strongly retained by the blood, 32 per cent remaining after half an hour and 25 per cent after fourteen days. In general, the crystalloid fraction was rapidly taken up by the tissues, but also rapidly excreted. The colloid fraction showed prolonged retention, 35 per cent still remaining after fourteen days. The whole drug tended to follow the pattern of the colloid fraction.

Neoarsphenamine behaved in an essentially similar manner, except that the colloid fraction was even more persistently retained. Blood concentrations were, whole drug 23 per cent after half an hour, disappearing at six hours or longer; crystalloid fraction 28 per cent after half an hour, 5.5 per cent after fourteen days; colloid fraction 33 per cent after half an hour, 20 per cent after fourteen days. Total retention of neoarsphenamine was 92 per cent after half an hour, 45 per cent after six hours, 22 per cent after twenty-four hours, and 8 per cent after fourteen days for the crystalloid fraction; the corresponding figures being 99 per cent, 72 per cent, 59 per cent, and 50 per cent for the colloid fraction, and 94 per cent, 65 per cent, 15 per cent and 3 per cent for the whole drug.

The acute toxicity of 4:4′-diamidino diphenoxy pentane and 4:4′-diamidino stilbene. L. D. SEAGER, J. N. ETTELDORF (by invitation), N. P. GRENFELL (by invitation), R. I. HEWITT (by invitation) and A. P. RICHARDSON. *Depts. of Pharmacology and Preventive Medicine, Univ. of Tennessee Medical School, Memphis, Tenn.* The acute toxicity of 4:4′-diamidino diphenoxy pentane (I) and 4:4′-diamidino stilbene (II) has been studied in dogs, cats, rabbits, and mice. In mice the intravenous LD_{50} of (I) was 12.1 ± 1.1 mgm. per kilogram and (II) was 13.5 ± 0.8 mgm. per kilogram. The LD_{50} of these drugs by oral administration was for (I) 486 ± 9.3 mgm. per kilogram for (II) it was 382 ± 21.0 mgm. per kilogram.

The intravenous injection of these drugs in a dose of one mgm. per kilogram produced the following circulatory changes. There was a precipitous fall in blood pressure of approximately 50 mm. of mercury. The blood pressure returned to normal in from three to four minutes. The fall in pressure was associated with an increase in leg volume, a decrease in cardiac volume, and a slight increase in pulse rate. Similar effects were produced in atropinized and spinal animals. Perfusion of the kidney with intact nerve supply was carried out according to the method of Sollmann and Pilcher. The systemic administration of (I) had no effect on blood flow through the isolated kidney, however, perfusion of (I) in a concentration of 1:1,000,000 produced a marked increase in rate of flow through the isolated kidney. It is concluded that (I) and (II) produce circulatory collapse, by direct depression of the peripheral vascular system.

The exposure of (II) to ultra violet light results in a substance which has a decreased fluorescence and a marked increase in toxicity. [*The work described in this paper was done under a contract, recommended by the Committee on Medical Re-*

search, between the Office of Scientific Research and Development and the University of Tennessee.]

Influence of post-pituitary extract on the polyuric response of white rats exposed to low barometric pressure. HERBERT SILVETTE. *Dept. of Pharmacology, Univ. of Virginia, Charlottesville.* It has been demonstrated that rats exposed to a pressure of 428 mm. Hg (15,000 ft. altitude equivalent) in a low-pressure chamber for 3 hours invariably develop polyuria (Proc. Soc. Exper. Biol. and Med. **51:** 199, 1942). This has now been shown to hold true regardless of the preliminary water-load of the animals, from 0 to 10 per cent body weight of injected fluid.

Experiments have been made to determine the effect of the injection of post-pituitary extract on the polyuria of high altitudes. In fully-fed animals injected with 5 cc. 0.2 per cent NaCl solution, the 3-hour urine excretion at room pressure averaged 2.1 cc. Animals similarly injected but exposed for 3 hours to 428 mm. Hg pressure excreted on an average 5.0 cc. urine. Other animals, similarly treated but with the addition of post-pituitary extract and then exposed to low pressure, averaged only 1.9 cc. urine, thus indicating that the polyuria of high altitudes was inhibited by the antidiuretic hormone.

Other animals were treated as follows with weekly rest periods between experiments: Pre-inary fasting period 12 hours with water allowed lib. Animals injected with 10 cc. per 100 grams .2 per cent NaCl solution with or without post-pituitary extract, and 3 hours later exposed either to room pressure or to 428 mm. Hg pressure during a metabolic period of 3 hours. Results may be tabulated as follows:

No. rats	Post-pituitary extract	3-hour urine output at 0 feet	3-hour urine output at 15,000 feet
	units/100 gm. BW	*cc./100 gm. BW*	*cc/100 gm. BW*
36	0	3.9	5.0
36	1	0.7	1.7

It will be noted that the injection of the extract reversed the high-altitude polyuria, and further that the water retention brought about by equal doses of post-pituitary extract, either at 0 or 15,000 feet, was almost exactly the same, i.e., 3.2 cc. at room pressure and 3.3 cc. at 428 mm. Hg. [*This investigation had been made with the assistance of a grant from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.*]

Blood levels of sulfonamide after intraperitoneal injection of a 50 per cent suspension of sulfanilamide in propylene glycol. F. W. SINGER (by invitation), C. J. SMYTH (by invitation) and F. F. YONKMAN. *William J. Seymour Hospital and Dept. of Pharmacology, Wayne Univ., Detroit.* A syrupy suspension of 50 per cent sulfanilamide in propylene glycol was injected intraperitoneally in varying amounts in five patients. Discomfort varying from a very slight to a moderately severe degree followed injection for three to ten minutes. This was almost entirely rectified by addition of 10 per cent benzyl alcohol, the patient describing his sensation as "heaviness", a "mild cramp" or "slight bellyache" for a matter of seconds. Blood levels of sulfanilamide in mgm. per cent, determined at regular intervals after varying doses of the suspension had been injected were as follows: After 20 cc. (10 grams sulfanilamide) in 3 patients, 1 hr. 13 to 25, 3 hr. 11 to 33, 6 hr. 16 to 26, 12 hr. 12 to 23, 24 hr. 8 to 14; after 15 cc. (7.5 grams sulfanilamide) in 2 patients, 1 hr. 4 to 5, 3 hr. 5 to 7, 6 hr. 5 to 5, 12 hr. 2 to 4, 24 hr. 2 to 7.

These results suggest that a dose of 15 cc. of the suspension (7.5 grams of sulfanilamide) seems to be a desirable quantity to employ for concentrated bacteriostatic medication of the peritoneal cavity since blood levels indicate that the sulfanilamide is maintained in the blood stream at safe levels and does not become elevated as may be the case after higher dosage.

An advantage of this preparation attends the fact that it is self-sterilizing (Fed. Proc. 1: Part II, 172, 1942) and can be readily injected at regular intervals either postoperatively, if indicated, or in non-surgical treatment of peritonitis.

The biological interference of thiopantothenic acid and pantothenic acid. E. E. SNELL, L. CHAN, S. SPIRODANOFF and E. L. WAY (by invitation) and C. D. LEAKE. *Chemical Labs. of the Univ. of Texas, Austin, and Pharmacology Laboratory of the Univ. of California Medical Center, San Francisco.* It is now clear that compounds with close chemical configuration may compete with each other in reactions with cell constituents, thus altering cellular function in varying ways. Initial English observations on interference of sulphonamides with p-amino benzoic acid have been extended by reports like McIlwain's (Brit. J. Exper. Path. 21: 136, 1940), which shows that pyridine-sulfonic acid interferes with nicotinic acid metabolism in micro-organisms, and Snell's (J. Biol. Chem. **141:** 121, 1941), which notes that the sulfonic acid, N-(α, λ -dihydroxy-β,β-dimethylbutyryl) taurine, or thiopantothenic acid, is structurally so similar to pantothenic acid that it interferes with the metabolism of the latter in micro-organisms.

We find thiopantothenic acid to be relatively inactive on single oral or intraperitoneal administration to small animals. No effects are noted from single doses as high as 2 grams per kilo in mice and rats. However, on long continued daily oral administration of thiopantothenic acid in mice at a

dose level of 200 mgm. per kilo, evidence of pantothenic acid deficiency appears. Within a month of such daily administration, on an otherwise adequate diet, growth in standard strains of laboratory mice becomes stationary, the hair becomes roughened, and porphyrin deposits show on the whiskers. Characteristic behavior symptoms develop, similar to those observed in direct pantothenic acid deficiency.

The production of hyposthenuria in dogs by desoxycorticosterone acetate. CLIFFORD SPINGARN (by invitation), MICHAEL G. MULINOS and ESTHER MACULLA (by invitation). *Dept. of Pharmacology, College of Physicians and Surgeons, Columbia Univ., New York City.* Small daily doses of desoxycorticosterone acetate (DCA) injected into normal dogs induce polydipsia and polyuria which are roughly proportional to the amount of NaCl allowed in the diet. Pitressin reduces the severity of the syndrome and raises the specific gravity of the urine but does not restore the water exchange to pre DCA levels (Am. J. Physiol. 135: 102, 1941). Furthermore, water deprivation fails to raise the specific gravity of the urine to normal levels.

The following experiments were performed on dogs before and during DCA injections, to determine any changes on fluid balance and urine specific gravity: a. Water and food deprivation for 48 hours. b. Partial water deprivation for several days sufficient to cause intense thirst. c. Daily injections of pitressin tannate in oil for periods of 8 to 13 days.

Results. Normal dogs treated with DCA increased their daily water intake from 174 to 1936 cc.; their urine output from 188 to 1869 cc. with a fall in specific gravity from 1.045 to 1.0054.

Under test a, the urine output was 125 cc. with a specific gravity of 1.054 for 48 hours before DCA and 350 cc. specific gravity 1.024 under DCA.

Under test b, the dogs were allowed 125 cc. of water per day and put out 140 cc. of urine of specific gravity 1.055; while under DCA they were allowed 267 cc. daily and put out 340 cc. of urine of specific gravity 1.027.

Under test c, the dogs drank 131 cc., put out 165 cc. of urine of specific gravity 1.054 while under DCA they drank 1147 cc., put out 1084 cc. of urine of specific gravity 1.0106.

From these results it is concluded that DCA affects the concentrating power of the kidney adversely. The hyposthenuria produced by DCA accounts in part for the polyuria and polydipsia induced by this drug.

The acute toxicity of vapors of benzene, tollac, velsicol no. 2 and toluene. J. L. SVIRBELY (introduced by W. F. von Oettingen). *Division of Industrial Hygiene, National Inst. of Health, Bethesda, Md.* About 650 white mice in groups of 16 or more were exposed for 7-hour periods to vapors of benzene, tollac, velsicol, toluene, and a mixture containing 60 per cent benzene plus 40 per cent toluene by weight. Values for concentrations were calculated in milligrams per liter by dividing the weight of the solvent vaporized by the amount of air used. These values were in close agreement with the vapor concentration in the exposure chamber as measured by the Rayleigh-Jeans Interference Refractometer.

Within 8½ hours from the beginning of exposure the concentrations in milligrams per liter killing 50 per cent of the animals were: benzene 33.1; tollac 27.0; velsicol 26.9; benzene-toluene mixture 24.60 and toluene 19.90. The approximate equivalents in parts per million of these solvents in the same order are: 10,400; 7,980; 7,580; 7,200 and 5,300.

Tollac and velsicol no. 2 are solvents consisting of a mixture of benzene and toluene with a small percentage of other hydrocarbons.

Effect of cocaine on the esterification of phenol. CLARA TORDA (introduced by McKeen Cattell). *Dept. of Pharmacology, Cornell Univ. Medical College, New York City.* Richter's theory regarding the inactivation of epinephrine by esterification of the phenol ring suggested the desirability of investigating the effect of cocaine on the esterification of phenol.

Phenol is conjugated in the body by phenol sulfur esterase. *In vitro* experiments with phenol sulfur esterase extracted from cat muscle showed that cocaine decreases the activity of this enzyme by about 50 per cent.

In vivo experiments confirm this result. Two groups of experiments were performed: In the first series phenol (5 mgm. per kgm.), with or without cocaine (15 mgm. per kgm.), was injected subcutaneously in fasting cats and the phenol excretion in 24 hour samples of urine determined. Cats injected with cocaine eliminated free phenol to the same extent as those without cocaine, but phenol in conjugated form was no longer eliminated, indicating that cocaine depressed the esterification of phenol. In the second series of experiments cats were injected continuously with small amounts of phenol (rate of 1.6 mgm. per kgm. in 30 min.) with or without cocaine (rate of 0.6 mgm. per kgm. in 30 min.). The phenol content of urine, collected from the ureters over 30 minute periods, was determined. Cocaine even in small doses (less than 0.6 mgm. per kgm.) inhibited the esterification of phenol.

The above results lend support to the theory of Richter that the body disposes of epinephrine, at least partially by esterification of the phenol ring.

Inhibition of the cardio-inhibitory action of acetylcholine by digitalis. J. A. WELLS (by invitation), CARL A. DRAGSTEDT, J. E. RALL (by invi-

tation) and D. A. RUGE (by invitation). *Dept. of Pharmacology, Northwestern Univ. Medical School, Chicago.* Numerous investigations have been performed in attempts to explain the cardiac slowing induced by digitalis. It is suggested that this slowing has both "vagal" and "non-vagal" components. The vagal component is variously ascribed to (1) direct stimulation of the vagus center, (2) reflex vagus action consequent to the cardiac action, (3) sensitization of the heart to the vagus mechanism. This latter concept implies that the sensitivity of the heart to acetylcholine is increased by digitalis. On the contrary, we have observed in anesthetized dogs that small doses of digitalis (approximately 10 per cent of the fatal dose) promptly prevent the response of the heart to a previously effective cardio-inhibitory dose of acetylcholine bromide (ca. 0.02–0.06 mgm. per kilo). In certain experiments subsequent injection of larger doses of acetylcholine now produced cardiac inhibition, but in other experiments even 10 times the initial dose produced no slowing. The vasodilator action of acetylcholine was not abolished

These findings are inconsistent with the hypothesis of an increased sensitivity of the heart to the vagus mechanism, and difficult to reconcile with the idea that any of the cardiac slowing is mediated by way of the vagus

Further studies have shown that this phenomon does not occur when strophanthin is given in ses up to 50 per cent of the lethal dose.

Whatever the ultimate explanation of these findings may be, they indicate that there is a qualitative difference in the cardiac effect of different cardiac glycosides.

Pharmacodynamics of the urine of patients with migraine. HAROLD G. WOLFF and CLARA TORDA (by invitation). *Dept. of Medicine and Psychiatry, Cornell Univ. Medical College, New York City.* Under suitable laboratory circumstances, the urine of healthy adult humans contracts the rectus abdominis muscle of the frog. Urine collected during the prodromic period (sctotoma) of a migraine attack contracts the rectus abdominis muscle less than samples collected during attack-free periods, and urine collected during the headache contracts the muscle more (about 200 per cent). The seventeen ketosteroid content of the urine parallels this contraction producing effect as demonstrated by chemical determinations and biological experiments. The gonadotropic hormone of hypophysis may contribute to this effect by itself or through an increased liberation of the sex hormones. This increased ability of the urine collected during migraine headache attack to produce muscle contraction is probably not due to potassium, acetylcholine, histamine, pitocin (antidiuretic hormone of posterior part of hypophysis, Parke-Davis), or is it related to the specific gravity of the urine. From the above observations and from the fact that the above hormones potentiate the effect of certain vasodilator substances, such as acetylcholine, it is conceivable that these hormones participate in the production of the migraine headache attack by potentiation of the effect of a local neurohumoral vasodilator agent.

Effects of posterior pituitary extract, oxytocin (pitocin) and ergonovine hydracrylate (ergotrate) on intra-uterine, arterial, venous and maternal effective placental arterial (MEPAP) pressures in pregnant humans. R. A. WOODBURY, B. E. ABREU, W. F. HAMILTON, and (by invitation) R. TORPIN and P. H. FRIED. *Depts. of Physiology and Pharmacology and Obstetrics and Gynecology, Univ. of Georgia School of Medicine, Augusta.* Pressures were determined by techniques previously described (Am. J. Physiol. 121: 640, 1938; 128: 238, 1940).

Prior to the onset of true labor, each 5–10 minutes the uterus contracts slowly to develop a pressure averaging 18 mm. Hg and relaxes to a resting tone of 5 mm. Hg. Ergotrate 0.1 mgm. or posterior pituitary preparations 0.7 unit, employed to induce labor, increased uterine frequency 80 per cent, rate of upstroke 100 per cent, pressure at height of contraction to 50 mm. Hg and tone to 15 mm. Hg. Repeated administrations sometimes produced incomplete tetany with maximal pressure during contractions of 60 mm. Hg and tone of 50 mm. Hg.

During the first stage of labor, ergotrate 0.1 mgm. or posterior pituitary preparations 2 units sometimes produced incomplete tetany and increased uterine frequency 75 per cent, tone from 12 to 40 mm. Hg and the maximal pressure at the height of contraction from 45 to 90 mm. Hg. The uterine pressure remained as high between contractions as the maximum during contraction without oxytocics.

Normal uterine contractions intermittently empty the extensive vascular area of a large volume of blood by a pumping action and increase venous pressure 4 mm. Hg. Cardiac output is probably increased temporarily and this may partly explain the increased systemic arterial pressure and pulse pressure. Despite the elevated arterial pressure (12 mm. Hg elevation) the high uterine pressure tends to keep blood from reaching the placenta; the MEPAP is reduced.

Abnormal contractions produced by oxytocics cause prolonged dangerous reductions in the size of the placental vascular reservoir and in the MEPAP. In one patient oxytocics reduced the MEPAP to +30/−20 mm. Hg indicating that blood flowed from the uterus back into the aorta during diastole.

Pitocin lowers the MEPAP even further since it actually decreases the maternal arterial pressure

and contains very little vasopressor principle. [*This work was aided by a grant from Eli Lilly and Company.*]

The effects of some new antispasmodics on the intestine of trained, unanesthetized dogs. F. F. YONKMAN, H. F. CHASE (by invitation), A. J. LEHMAN and R. BAUER (by invitation). *Dept. of Pharmacology, Wayne Univ., Detroit.* Several new antispasmodics of the morpholine type which were synthesized by the Parke Davis Research Division were administered intravenously and directly into stomata of the ileum or colon of eight trained, unanesthetized dogs. Changes in intestinal motility were recorded kymographically as they were transmitted by the well-known closed system of balloon-manometric registration. For purpose of comparison Trasentin was chosen as a standard and this drug was administered by the same routes used for the new synthetic unknowns.

Intravenous administration of the five S-compounds studied in this series usually caused nausea and frequently resulted in vomiting but in the experiments in which the unknowns were inserted into the intestine, S-29 (ω-(4 morpholine)-hexyl diphenylacetate HCl) was the most outstanding. It produced better and more consistent relaxation than the others. It was slightly less enduring than Trasentin in its action, e.g., 10 mgm./kgm. of S-29 inserted into the intestine in a 1 per cent solution produced relaxation for approximately one to two hours, whereas relaxation produced by similar doses of Trasentin endured usually for one and one-half or two hours or more. Peristalsis was lessened and segmental movements were diminished in frequency and amplitude by both S-29 and Trasentin.

Since our M.L.D.$_{50}$ dose of S-29 after intraperitoneal injection into white mice (475 mgm. per kgm.) is more favorable than our figure for Trasentin (200 mgm. per kgm.) clinical trial is anticipated using Trasentin as a standard.

THE AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY

Abstracts of papers presented for the annual meeting scheduled for Cleveland, April 6–10, 1943. On account of the cancellation of this meeting, all the papers are to be regarded as "read by title." For possible correction in any of the abstracts see the next issue.

Hematic and organic reactions in standardized and graded histamine shock in dogs. W. C. HUEPER and C. T. ICHNIOWSKI (by invitation). *Warner Institute for Therapeutic Research, New York City.* Dogs were injected subcutaneously with single doses of 5. mgm 10 mgm., 15 mgm., and 20 mgm. of histamine dihydrochloride suspended in an oily vehicle (cottonseed oil 3 parts, "Falba" 1 part). The blood pressure was gradually lowered to a level of 20–40 mm. of mercury for several hours. The duration of the depression of the blood pressure, shortness of survival period and the mortality rate increased with the dose of histamine dihydrochloride given. Dogs dying during the first 7 hours showed a dilated heart and evidence of a cardiac death; those dying later had a contracted left heart and showed signs of a circulatory failure by increased capillary permeability. Appreciable hemoconcentration was not a characteristic hematic manifestation. Decrease of erythrocytes was noted not infrequently, particularly 24 hours after the histamine administration. The plasma viscosity decreased only mildly to moderately during shock, while the colloidal osmotic pressure of the serum determined at hourly intervals increased considerably. Gastric ulcers were present in an appreciable number of dogs within 7 hours after the injection.

Methods for the production of a standardized and graded secondary shock in animals are essential for a study of the dynamics of shock and for the testing of therapeutic agents used in the management of this condition.

"Exploded" red blood cells in miliary lesions of the bone marrow. RAPHAEL ISAACS. *Michael Reese Hospital, Chicago.* In making blood films of patients with miliary lesions of the bone marrow (neoplasms, tuberculosis, leukemia) an artifact of some of the red cells is produced. These cells have a round center, with projections from the periphery which takes the same stains as hemoglobin. The cells are tougher than normal, and instead of responding to the pressure when the film is made, the surface ruptures in a number of places and hemoglobin containing material exudes. This gives the appearance of an intact cell, with numerous projections of different shapes, lighter in color. The artifact appears when there is a crowding lesion of the bone marrow in miliary form, not in discrete masses.

On the mechanism of cellular injury in inflammation. VALY MENKIN. *Dept. of Pathology,*

Harvard Univ. Medical School, Boston, Mass.
An attempt has been undertaken to determine the factor responsible for the basic pattern of injury in the development of inflammation. It is true that the irritant induces initial cellular injury; but the available data strongly supports the view that the subsequent course of events is primarily referable to the liberation of a euglobulin or at least of a factor associated with the euglobulin fraction of exudates. The salient findings may be briefly listed as follows: 1) An inflammatory exudate injected into rabbits induces a severe edematous inflammation accompanied by lymphatic blockade; 2) either dialysis or fractionation of exudative material with ammonium sulfate at one third saturation yields in the euglobulin fraction a substance capable of inducing a marked, erythematous and frequently necrotizing inflammation; 3) The injection of this active protein fraction promotes lymphatic blockade; 4) The effect cannot be duplicated with the euglobulin recovered from normal blood serum, but the euglobulin of the serum from an animal with a concomitant severe inflammation frequently displays injurious potency; 5) The effect cannot be reproduced by the pseudoglobulin or albumin fractions of exudate; 6) The substance injected into the circulation induces a leukopenia in dogs; 7) It fails to depress the blood pressure of a cat; 8) It hastens the coagulation of blood *in vitro* (perhaps due to the presence of adhering thrombokinase); 9) The name "*necrosin*" has been assigned to this protein which is *per se* capable of reproducing the basic pattern of injury in inflammation.

The effect of the leukocytosis-promoting factor on the growth of cells in the bone marrow. VALY MENKIN. *Dept. of Pathology, Harvard Univ. Medical School, Boston, Massachusetts.* The earlier studies of the writer have demonstrated the presence of a leukocytosis-promoting factor in inflammatory exudates. The factor has been shown to be apparently a pseudoglobulin. It offers a reasonable explanation for the mechanism of leukocytosis accompanying numerous inflammatory processes. It is absent in normal blood serum, but it can be recovered from the latter if there is a concomitant inflammation. The rise in the number of circulating leukocytes consists primarily of immature granulocytes. The evidences indicate that the leukocytosis-promoting factor penetrates into the blood stream from the site of inflammation and thus reaches the bone marrow, where it induces a discharge of leukocytes into the circulation. The present study demonstrates that this active pseudoglobulin not only causes such a discharge of cells from the bone marrow, but that it also induces a pronounced hyperplasia of myeloid elements and of megakaryocytes in the hematopoeitic tissue of the marrow. The effect cannot be reproduced by the pseudoglobulin extracted from normal serum. A similar hyperplastic response in the bone marrow can be affected by injection of the whole exudate or by inducing an acute inflammation in the pleural cavity of dogs. The leukocytosis-promoting factor, derived from either dog exudates or from human exudates injected into the circulation of dogs, induces marked hyperplasia of the bone marrow. The clinical implications as well as the pathological significance of these observations are obvious.

Attempts to abrogate immunity to the Brown-Pearce carcinoma. OTTO SAPHIR and MAX APPEL (by invitation). *Department of Pathology, Michael Reese Hospital.* Rabbits were immunized to the Brown-Pearce carcinoma by intracutaneous transplantation as described by Gross and Besredka, and others. The effect of trauma on the immunity established in this manner was investigated by subjecting the immune animals to trauma applied as follows:

(1) Multiple needle-puncture wounds were made in liver and kidneys, and a suspension of tumor cells injected intravenously (6 rabbits).

(2) Both bones of the left fore-leg were fractured and a suspension of tumor cells injected intravenously (12 rabbits).

Three normal control rabbits were injected intravenously with the same suspension of tumor cells. All of the control animals developed tumor, proving that the tumor cells in suspension were viable, whereas, none of the immune animals subjected to trauma developed tumor.

The effect of partial blockade of the reticuloendothelial system was then studied. Twelve rabbits were immunized by intracutaneous injection of the tumor. Nine of them were then given 3 daily intravenous injections of 3 cc. of 0.1 per cent trypan blue in saline. Subsequently all 12 were injected intravenously with a saline suspension of tumor cells. Trypan blue was continued for another two weeks. The three which did not receive trypan blue prior to injection remained free of tumor. Of the 9 which did receive prior injection of the dye, seven developed tumors in kidneys, liver and lungs. A striking feature of the tumors developing in these previously immune animals was the marked necrosis.

Observations on the kinetics of cellular cathepsin. II. From organs of normal rabbits and those infected with virulent and non-virulent tubercle bacilli. CHARLES WEISS and (by invitation) NELLIE HALLIDAY. *Research Laboratories of the Mount Zion Hospital, San Francisco, Calif.* Since the investigations of Opie and those of our own laboratories have emphasized the important role played by proteolytic enzymes in inflammatory processes, we studied the behavior of the cellular proteinase, Cathepsin II, extracted from

the organs of normal rabbits, those infected with non-virulent tubercle bacilli as well as from those thus treated and then reinfected with a virulent (Ravenel) strain of *M. tuberculosis*.

The analytical procedures of Fruton and Bergmann were employed in studying enzyme reaction kinetics, using the substrate benzoyl-l-arginine-amide (BAA). The speed with which normal rabbit tissue enzymes hydrolyze this substrate is, correlated with the bactericidal power (for virulent tubercle bacilli) of the organs from which they were extracted. Spleen > liver > kidney > lung is the order of activity. Reinfection *via* the blood stream with virulent tubercle bacilli, after immunization with a non-virulent strain, causes an increased activity rate of Cathepsin II, particularly that from the kidneys and lungs. Repeated inoculation and sensitization with a non-virulent (R_1) strain causes a mild decrease in speed of hydrolysis of enzymes extracted from spleen, liver and kidneys and a slight increase in those of the lungs. Hence, the mobilization and intensification of the activity of cellular cathepsin may be a phase of the altered biochemical characteristics of allergic and immune animals. Those organs (kidneys and lungs) which presumably benefit most from immunization and reinfection processes show the development of a greater speed of proteolysis than those (liver and spleen) which already have a satisfactory degree of natural immunity.

THE AMERICAN INSTITUTE OF NUTRITION

Abstracts of papers presented for the annual meeting scheduled for Cleveland, April 6–10, 1943. On account of the cancellation of this meeting, all the papers are to be regarded as "read by title." For possible correction in any of the abstracts see the next issue.

The nutritive value of soybean proteins. GLADYS J. EVERSON, HARRY STEENBOCK, HELEN T. PARSONS and DENA CEDERQUIST. *Depts. of Biochemistry and Home Economics, College of Agriculture, Univ. of Wisconsin.* Studies on the nutritive value of soybean proteins as carried out with rats revealed that the improvement effected by autoclaving was a common property irrespective of the cystine or sulfur content of different varieties. It was not the resultant of the destruction of toxic compounds nor apparently solely, if at all, to an improvement in digestibility.

Five different protein fractions were prepared by extraction with NaCl followed by dialysis. All of these were improved in nutritive value by autoclaving at 17 pounds pressure for 15 minutes. One of the globulin fractions prepared at low temperatures and then treated with dilute acid, dilute alkali, urea or hydrogen peroxide had the same nutritive value as the untreated fraction prepared at 28°C.

Germination of soybeans produced an improvement which was almost equivalent to that produced by the addition of cystine or by autoclaving. Green, immature soybeans were superior in nutritive value to ripe soybeans though inferior to either autoclaved.

Nutrition and tolerance to atabrine. D. M. HEGSTED (by invitation), J. M. MCKIBBIN (by invitation), and F. J. STARE. *Division of Nutrition, Dept. of Biochemistry, Schools of Medicine and Public Health, Harvard Univ., Boston.* This paper is a preliminary report of investigations designed to study the rôle of nutrition in the ability of various experimental animals to tolerate the continued administration of the antimalarial drug atabrine.

One hundred and thirty white rats weighing 30 to 40 grams each were placed on a purified diet. The diet contained adequate but not excessive amounts of the vitamins. Atabrine dihydrochloride was fed in levels varying from 1.0 to 65 mgm. per kilogram body weight per day. At levels of 25 mgm. per kilogram or less and over a period of five months, no effects of atabrine were noted other than a mild yellowing of the skin. Growth was the same as the controls, pathologic examinations were negative. At a level of 40 mgm./kgm. growth rates were approximately 15 per cent less and at 65 mgm./kgm. they were 25 per cent less. At these levels of atabrine the skin and all body tissues except brain and nerve were markedly pigmented. The hair coat presented an untidy appearance. Food consumption was approximately the same as the control animals on a body weight basis. Increasing the water soluble vitamins five fold, or addition of yeast to the extent of 4 per cent, did not affect the growth retardation caused by continued high amounts of atabrine.

This indicates that the healthy young rat on an adequate diet is remarkably tolerant to amounts of atabrine which are large in comparison to that used in suppressive, prophylactic, or therapeutic therapy in man.

Complete parenteral nutrition. J. M. McKibbin (by invitation), D. M. Hegsted (by invitation) and F. J. Stare. *Division of Nutrition, Dept. of Biochemistry, Schools of Medicine and Public Health, Harvard Univ., Boston.* Adult dogs receiving only water orally were infused with mixtures containing all the nutritional factors known to be required by dogs. Two types of mixtures were used. One contained a casein hydrolysate ("Amigen") with glucose, calcium, magnesium, "trace" elements and water-soluble vitamins. The other contained corn oil in emulsion with a stabilizer, glucose, sodium, potassium, chlorine, phosphorus, "haliver oil," vitamin K, and choline. They were infused in amounts of 18 and 40 ml. per kilogram of body weight per day, respectively. The total daily caloric intake was calculated to be about 40 calories per kilogram. No pyrogenic effects were observed in the use of these mixtures but occasionally there was nausea and vomiting.

When the corn oil emulsion was stabilized with commercial soybean lecithin (3.5 per cent corn oil and 3.5 per cent lecithin) without choline, very severe liver damage was observed after 12 to 18 days with the development of jaundice and splenomegaly. Lowering the concentration of lecithin to 0.7 per cent, with the corn oil at 6.3 per cent, and adding choline produced after 18 days the same character of liver damage but in considerably milder form. No jaundice or splenomegaly resulted.

Infusion of a 7 per cent lecithin emulsion alone with the oral feeding of an adequate ration resulted in mild liver damage in 30 days and a greatly enlarged spleen accompanied by a continued fall in the hematocrit and marked posterior paralysis. Studies on the use of other emulsion stabilizers are in progress.

THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS

Abstracts of papers presented for the annual meeting scheduled for Cleveland, April 6–10, 1943. On account of the cancellation of this meeting, all the papers are to be regarded as "read by title." For possible correction in any of the abstracts see the next issue.

Studies of the site of antibody formation in bbits following intracutaneous injections of neumococcus or of streptococcus vaccine. Paul F. de Gara and D. Murray Angevine. *Dept. of Pathology, Cornell Univ. Medical College, New York City.* Within 5 to 12 days following a single injection of the vaccines, high antibody titres were detected in extracts from the site of the injection into the skin, the spleen, bone marrow and liver. Antibodies were also found in draining lymph nodes. During this period the serum titre was low or negative. When the interval was prolonged, the titres of the blood and of the organs showed but slight differences. High titres were observed in the injected skin. Titrations after a still longer interval showed that the serum titre decreased more rapidly than the titre of the spleen, bone marrow and injected skin.

Similar results were obtained following repeated injections of vaccines. However, antibodies usually were not detected during the first period in the injected skin and were not found in the lymph nodes of these rabbits.

The antibody titre of the kidney, anterior wall of the stomach and non-injected parts of the skin was negative or low.

The presence of antibodies at the site of the injection of the antigen and in the spleen, bone marrow, liver and lymph nodes before they appeared in the blood and in other organs suggests that antibody formation takes place in those tissues.

Liver and spleen that showed high titres frequently gave marked antigen-antibody reactions *in vivo*. The titres of kidney and anterior wall of the stomach were low or negative, and reactions *in vivo* were observed less frequently and were less marked than those in liver and spleen.

Tissue reactions in internal organs of rabbits intracutaneously sensitized with streptococcus or with pneumococcus vaccine to injections of the homologous antigen. Paul F. de Gara and D. Murray Angevine. *Dept. of Pathology, Cornell Univ. Medical College, New York City.* Homologous vaccine was injected after various intervals into abdominal organs of rabbits that had been sensitized intracutaneously with heat-killed pneumococci Type I or with formalin-killed hemolytic streptococci.

Local reactions showing varying degrees of inflammation with or without necrosis were observed in the liver and spleen of approximately 70 per cent of the rabbits. Injections into the kidney and anterior wall of the stomach usually caused hemorrhagic lesions at the site of injection, frequently

accompanied by a slight to moderate inflammatory reaction; more severe necrotic reactions occurred in only 2 of 25 kidneys and in 2 of 10 stomachs.

The reactions in the liver and spleen are probably the result of the union within the tissues of antibody with its specific antigen.

The antigen-antibody reactions observed *in vivo* are in agreement with our recent experimental work showing a high antibody titre of saline extracts of the same organs, namely, liver and spleen.

There was no correlation between the reactivity of the skin and the reactivity of the internal tissues to the vaccines of rabbits previously sensitized by intracutaneous injections of the homologous antigen.

A test for the action of drugs in vitro on the agent of lymphogranuloma venereum. HELEN JONES (by invitation) and GEOFFREY RAKE. *Division of Microbiology, The Squibb Institute for Medical Research, New Brunswick, N. J.* A strict *in vitro* technique was desired in testing, against the agent of lymphogranuloma venereum, prophylactics possibly effective against all venereal diseases. Such a test might indicate clinical efficacy during the important period before invasion of tissues has occurred. Unless an attempt is made to remove drug from the inoculum, even where small amounts of drug are incubated with the agent, tests must be considered as *in vivo*.

We use yolk-sac inoculation of chick embryos, a technique of great delicacy in detecting minimal amounts of active agent. Given quantities of drug are incubated at 37°C. with approximately 500,000 infective units of the agent in broth for 1 or 3 hours. The drug-agent mixtures are then centrifuged 1 hour at 15,000 r.p.m. at 0°C. The sediment is resuspended in broth to the same volume, and centrifugation and washing are repeated twice more. The final sediment is resuspended in twice the original volume and 1 ml. inoculated into the yolk-sacs of six day embryos. Such manipulation does not impair the infectivity of the agent. Chemical analysis showed that 1.5 per cent or less of the original drug concentration remains in the inoculum. In most cases this amount was probably bound to the components of the sediment. Titration of activity *in vitro* by such a method gives reproducible results and a sharp break on varying the dilution five-fold or less. One can distinguish drugs, such as the arsenicals, which are active *in vitro*, from those having little if any activity except *in vivo*.

The production of brain antibodies in the monkey. LENORE M. KOPELOFF (by invitation) and NICHOLAS KOPELOFF. *Dept. of Bacteriology, New York State Psychiatric Institute and Hospital, New York City.* Previous attempts to produce brain antibodies in animal species other than the rabbit have proved unsuccessful. In our hands the favorable methods used for the rabbit have likewise failed in the monkey.

By adapting Freund's use of adjuvants, monkeys were injected intramuscularly with mixtures containing: residues of alcoholic brain extracts; a conveyor (egg-white, horse serum, or pig serum); *M. tuberculosis* or *phlei*; Aquaphor; and paraffin oil. Three 3-week courses of 6–9 injections each were administered to 7 monkeys, 4 of which survived.

Brain antibodies were demonstrable in serum dilutions ranging from 1:80 to 1:640 by the usual complement-fixation technic. The efficiency of the method of immunization was evidenced by the degree of precipitin formation specific for the proteins used as conveyors, which was considerably greater than that produced by ordinary methods in the monkey.

Positive complement-fixation reactions were obtained to the same degree with alcoholic extracts of monkey brain, sheep brain, and rabbit brain. Antigens prepared from alcoholic extracts of monkey liver, lung, spleen, heart, whole blood, plasma, and red blood cells gave negative reactions. Monkey testicle and rabbit kidney yielded some evidence of cross-reaction.

Five additional monkeys immunized similarly with extracts of sheep kidney or monkey red blood cells served as negative controls.

By means of a special method of immunization it has been possible to demonstrate brain antibodies in an animal species other than the rabbit, namely, the rhesus monkey.

The production of chronic nephritis in the rat following the initial injection of anti-placenta serum. II. Pathological findings. EMILY NICHOLS LOEB and BEATRICE CARRIER SEEGAL (introduced by A. R. Dochez). *Depts. of Medicine and Bacteriology, College of Physicians and Surgeons, Columbia Univ., New York City.* The injection of rabbit anti-rat-placenta serum into rats has resulted in renal insufficiency in over half of 28 animals tested. Six were sacrificed because of approaching renal failure and in 4 others unilateral nephrectomy was performed. In all 10 cases histological examination revealed marked nephritis in the excised kidneys as well as in those examined at autopsy. All were finely granular with narrowed cortex and pronounced tubular markings. Microscopically thickening of the basement membrane of Bowman's capsule and glomerular damage varying from swelling of the tuft to crescent formation and complete obliteration were present. Casts were numerous and, in many areas, tubular dilatation and flattening of the epithelium with actual cyst formation occurred. In 3 animals which progressed rapidly and which were sacrificed 3½ to 5 months following injection the kidneys were greatly enlarged and odematous.

Microscopically the most extensive damage was present. With the exception of possible vascular lesions, which await further study, the autopsy findings revealed no lesions outside of the kidney.

The control animals received rabbit anti-rat-kidney serum, rabbit anti-rat-serum serum and normal rabbit serum. Eight of 13 animals receiving rabbit anti-rat-kidney serum developed chronic nephritis indistinguishable histologically from that occurring in animals receiving anti-placenta serum. Since the prerequisite albuminuria has failed to develop in the other controls, these animals remain under observation.

The injection of rabbit anti-rat-placenta serum into rats initiates chronic nephritis which progresses, without subsequent injection, to renal insufficiency. This nephritis is indistinguishable from that following the injection of specific anti-kidney serum.

Induced penicillin resistance in a pneumococcus type III culture. C. M. McKee and C. L. Houck (by invitation). *Division of Microbiology, The Squibb Institute for Medical Research, New Brunswick, N. J.* A type III pneumococcus culture of high mouse virulence was subjected to serial passage in broth containing the greatest amount of penicillin just permitting growth. After 26 passages the culture grew in ten-fold the originally inhibiting concentration, and after 55 passages in thirty-fold concentration. The resistant culture grew more slowly and colonies on blood agar were smaller and less mucoid. The capsule was reduced in size and there was a slightly greater tendency to chain and clump formation with the occurrence of abnormal forms. Type specificity, as determined by the Quellung method, and bile solubility were retained. Sugar fermentation reactions occurred more slowly, but were otherwise unchanged. A great change in mouse virulence occurred. Before passage, approximately 10 organisms constituted a lethal dose. After 55 passages, constant death of mice could be achieved only with undiluted culture or approximately 900 million organisms. Virulence could not be restored even after 9 further mouse passages. Neither mouse passage nor rapid serial transfer in blood broth decreased this acquired resistance to penicillin *in vitro*. Three staphylococcus, a streptococcus pyogenes, and type I and III pneumococcus cultures subjected to the same procedure developed resistance in the order named. In every case increase in resistance was associated with proportional loss of virulence. This is in striking contrast to the retention of virulence by sulfonamide resistant cultures.

Quantitative serum-virus relationship in neutralization tests with western equine encephalomyelitis virus. Isabel M. Morgan (introduced by Peter K. Olitsky). *The Rockefeller Institute for Medical Research, New York City.* Antisera from rabbits vaccinated with repeated doses of active or formalin-inactivated chick-embryo Western virus were tested by intraperitoneal neutralization tests in young mice, using dilutions of antiserum and dilutions of active mouse-brain virus incubated 2 hours at 37°C. When the results were plotted on a log-log scale, with amount of virus neutralized on the ordinate and serum-dilutions on the abscissa, parallel straight lines were obtained with a slope greater than one. The serum-virus relationship was similar to that found for influenza virus (Horsfall, F. L., J. Exper. Med., 1939, 70: 209).

For intracerebral neutralization tests, however, rabbit antiserum-virus relationship was not linear; with increasing amounts of antiserum the curves at first rose steeply then flattened out. Thus for any given antiserum there was little or no difference between the amount of virus neutralized by undiluted and by 1/10 dilution of serum.

In contrast, dilutions of serum from men vaccinated with two doses of formalin-inactivated virus neutralized by cerebral test progressively larger amounts of virus as the amount of serum was increased, showing a linear relationship on a log-log scale with a slope greater than one. Far greater amounts of virus could be neutralized by undiluted human antiserum than by rabbit antiserum.

Thus a species difference between rabbit and human antisera was found in the quantitative serum-virus relationship as shown by intracerebral neutralization tests in mice with the virus of Western equine encephalomyelitis. The explanation for such a difference is being sought.

Immune response and delayed reactions in guinea pigs after serotherapy of equine encephalomyelitis virus infection. P. K. Olitsky, R. W. Schlesinger (by invitation) and I. M. Morgan (by invitation). *The Rockefeller Institute for Medical Research, New York City.* Most guinea pigs succumbed within 3 to 5 days after inoculation of Western virus into the hind pads. Occasional ones survived; recovery was associated with development of active immunity characterized by high titer of neutralizing antibody and by resistance to intracerebral inoculation of homologous virus. When hyperimmune rabbit serum was given intracardially to guinea pigs 24 to 48 hours after injection of virus, those which survived showed no evidence of active immunity: the titer of neutralizing antibody decreased at the same rate as in non-infected control animals which had received antiserum only. Several serum-treated guinea pigs came down with typical fatal encephalitis after unusually prolonged (13 to 47 days) incubation periods. These delayed reactions occurred at a time when serum-antibody had fallen to a low titer but was still demonstrable. It was

believed that the delayed reactions could not have been caused by virus reaching the CNS from the periphery at that time, since it would have been exposed to the action of antibody in the blood stream. More likely, virus persisted during the prolonged incubation period within the CNS. The concentration of antibody in this organ parallels, at a 1:300 ratio, that in the serum (Morgan, Schlesinger and Olitsky, J. Exp. Med., 1942, 76: 357). Thus, when a low serum—antibody titer was reached, the antibody content of the CNS became ineffective and could no longer prevent virus from passing to and infecting other cells.

The prophylaxis and treatment of experimental influenza by inhalation of immune serum.[1] THE PERSONNEL OF NAVAL LABORATORY RESEARCH UNIT[2] # 1. *University of California, Berkeley.* To test the efficacy of immune serum administered by inhalation (INH) for prophylaxis and treatment of experimental influenza we employ an atomizer which sprays a fine mist composed of approximately 2.7×10^{-2} ml. of fluid per liter of air delivered. Experiments on monkeys and mice with india ink and radioactive chromic phosphate as indicators have shown that inhalation results in uniform distribution and penetration to the outermost alveoli of the lungs, a result unobtainable by intranasal instillation (INST).

A globulin fraction of influenza immune horse serum administered to mice (INH) has been shown to reduce subsequent infection, the degree of protection increasing with the duration of inhalation. Immune serum (INST) and globulin (INH) were effective in the treatment of mice infected as long as 48 hours before treatment was instituted. Repeated treatments 24 hours apart were significantly more effective than one treatment.

Some degree of immunity was produced by repeated administration of formolized virus (INST) to mice, but when immune serum was given concurrently active immunity failed to develop. Neutral mixtures of immune serum and active virus (INST) did not produce measurable immunity over and above that ascribable to the immune serum.

Treatment of influenza immune horse serum with certain enzymes results in a product so reduced in antigenicity and altered in specificity that the likelihood of allergic reactions in humans is greatly reduced. Evaluation of despeciated immune serum as a prophylactic and therapeutic agent for experimental influenza is in progress.

Asphyxiated tubercle bacilli as a vaccine. TRUMAN SQUIRE POTTER. *Laby. of Preventive Medicine, Univ. of Chicago.* Many if not all parasites, in a moist state and at 38–45°C., may be killed by depriving them of oxygen supply, (J. Infect. Dis., December, 1942). This fact may be used to prepare vaccines. However, if dried or kept at low temperatures, the parasites may become immune to deprivation.

Human, bovine, or avian-type tubercle bacilli may be killed by merely shutting off their supply of *molecular* oxygen, without much attention to oxygen compounds. This does not hold good for anaerobic bacteria which subsist on oxygen compounds.

The oxygen deprival not only kills, but favors preservation of vaccine structure. After killing, the vaccine is best stored on dry ice, like other antigens.

The human-type tubercle bacilli, completely killed by incubation at 38°C. in moist vacuum tubes, may confer on guinea pigs a definite increase in survival time after human-type infection, comparable to that obtained by living vaccine heterologous in type (BCG). But the immunized guinea pigs eventually die as a rule.

Rabbits, like human beings, are naturally far more resistant to human-type bacilli than guinea pigs. In fact, large doses of bacilli, (0.1–0.5 mgm.), in rather coarse suspensions, are necessary to produce extensive morbidity. Even then recovery is the rule unless unusual factors intervene. In two series of rabbits the immunes, protected by 6 subcutaneous inoculations of approximately 13 mgm. doses of vaccine, almost completely escaped the morbidity occurring in controls. These controls were siblings, from closely inbred families. The morbidity consisted chiefly of lesions of the lungs, kidneys, oviducts, testes, and mammary glands.

The production of chronic progressive nephritis in the rat following the initial injection of specific anti-placenta serum. I. Clinical findings. BEATRICE CARRIER SEEGAL and EMILY NICHOLS LOEB (introduced by A. R. Dochez). *Depts. of Bacteriology and Medicine, College of Physicians and Surgeons, Columbia Univ., New York City.* We have reported that rabbit anti-rat placenta serum injected into pregnant rats causes degeneration of the placentae and foetal death. The present studies describe observations made over 10 months following the injection of rabbit anti-rat-placenta serum into male and female rats. Twenty-eight hooded animals 46 to 87 days old were injected intravenously on three successive

[1] The opinions advanced in this paper are those of the writers and do not represent the official views of the Navy Department

[2] The Unit Personnel consists of: Albert P. Krueger, Commander (MC) USNR., Officer-in-Charge, and L. E. Rosenberg, Lieut. USNR.; R. G. Welsch, Lieut. (MC) USNR.; N. S. West, Lieut. USNR.; A. S. Browne, Lieut.(jg) USNR.; O. J. Golub, Lieut.(jg) USNR.; A. H. Jacobs, Lieut.(jg) (MC) USNR.; J. R. Mathews, Lieut.(jg) USNR.; A. J. Glazko, Ens. USNR.; M. D. Thaxter, Ens. USNR.; H. M. S. Watkins, Ens. USNR., I. L. Shechmeister, CPhM, USNR.; W. L. Axelrod, PhM, 1c, USNR.; E. R. Chisholm, PhM, 1c, USNR.; G. B. Saviers, PhM, 1c, USNR.; P. J. Smith, PhM, 1c, USN.; H. R. Burkhead, PhM, 2c, USNR.; C. R. Webb, Jr. PhM, 2c, USNR.; J. A. Gray, Jr PhM, 3c, USNR.; D. D. Mentz, HA, 2c, USN.

days with a total of 1.25 to 2.0 cc. of rabbit anti-rat-placenta serum. Three separate serums, obtained by immunizing rabbits with perfused rat placentae, were tested.

Thirteen control animals injected with rabbit anti-rat-kidney serum, 2 with rabbit anti-rat-serum serum and 7 with normal rabbit serum were under simultaneous observation. All animals were on McCollum's stock diet.

The injection of rabbit anti-rat-placenta serum produced a constant albuminuria (5 to 20 gm. of albumin per liter in random samples tested) in 15 animals. Nine of the remaining animals have had marked albuminuria at times but it has not been constant. Four have escaped kidney injury as judged by the absence of albuminuria. Eight of the animals showing albuminuria had nitrogen retention with blood non-protein nitrogen values ranging from 50 to 190 mgm. per cent. Histological examination in 10 of the animals with albuminuria revealed a chronic nephritis which is described in the accompanying abstract. All 3 anti-placenta serums tested produced identical kidney lesions, irrespective of the sex of the animal.

Animals injected with rabbit anti-rat-kidney serum have run a course similar to that following rabbit anti-rat-placenta serum. The other controls have normal urines and no nitrogen retention.

All surviving animals remain under observation.

Conversion of antibodies into the "univalent" form. ALBERT TYLER (introduced by Michael Heidelberger). *Wm. G. Kerckhoff Laboratories of the Biological Sciences, California Institute of Technology, Pasadena.* It has been shown that, by means of heat, proteolytic enzymes, ultraviolet or x-radiation, fertilizin (the natural sperm agglutinin obtained from eggs of various marine animals) can be converted into a non-agglutinating but still specifically reacting form. In conformity with Heidelberger's and Marrack's theory that agglutinating or precipitating antibodies are multivalent in respect to their specific combining sites, the non-agglutinating form is termed univalent. Attempts were made to convert, by the above methods, immune agglutinins as well as the normal iso- and hetero-agglutinins in mammalian sera into the univalent form. Heat and ultraviolet irradiation were extensively tested on rabbit antisera vs. sea-urchin sperm and vs. sheep erythrocytes, on normal human sera and on beef sera. The former agent was found to be ineffective and the latter gave partial conversion along with considerable destruction of specific combining action. Another agent, photodynamic irradiation, the employment of which was suggested by the results of some early experiments by Fleischmann (Münch. Med. Wchnschr. 52: 693, 1905) was found to be highly effective. Eosin (0.1 to 0.5 per cent) was used as the photodye and the antisera were irradiated (fluorescent "daylight" lamps) just long enough to reduce the agglutinin titer to zero. Determination of the inhibiting action of the treated sera on agglutination by untreated sera was taken as the measure of the extent of conversion to the univalent form. In most cases the results show 50 per cent or more of the original combining power to be retained by treated antisera. Tests of the active antigenicity of the treated sera and on the ability of the univalents to act as hemolysins and as complement-fixing antibodies are in progress.

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CORRECTIONS OF ERRORS IN MARCH ISSUE

Page 45. Silver, Kelso and Steinhaus. Thirteenth line of abstract correct "to produce strength" to read "to produce stretch". Also eleven lines below this, last word, delete "in-.

SYMPOSIUM ON THE SPECIAL SENSES IN RELATION TO MILITARY PROBLEMS

HALLOWELL DAVIS, CHAIRMAN

Department of Physiology, Harvard Medical School

For many years the organs of special sense have been regarded by most physiologists merely as interesting appendages of the central nervous system. In fact, it has been an open question whether they fall within the province of physiology or whether they inhabit the no-man's land between physiology and psychology. It is worth noting that among our contributors to the present Symposium, at least three, although they are members of our Society, are better known as psychologists than as physiologists.

Modern warfare has suddenly re-emphasized for us the practical importance of the special senses and it is the recognition of this practical importance that has led to the selection of the topic of "The Special Senses in Relation to Military Problems" for our present Symposium. We wish to be informed of the state of our knowledge of vision, hearing, equilibrium and the rest, and also of the nature of those practical problems of military significance of which we are only vaguely aware. Unfortunately, our contributors cannot go as far as they might wish in bringing us detailed information of their present work because of the obvious limitations imposed by considerations of military security. In spite of the dearth of specific information on many topics, we may take comfort in the thought that many of the problems that may be discussed merely as problems have already been vigorously attacked, and we may look forward to the day when the results of present work can be published freely and made a part of our general scientific knowledge.

Our thanks are due the contributors who, in spite of the pressure of their war-time responsibilities, have taken the time and trouble to write articles for a Symposium that cannot be presented orally to the Society and from which they must perforce omit most of the current data the presentation of which would be of great interest to them. In fact, several of our members who were invited to contribute have felt that they could not offer anything worthwhile under the necessary present restrictions.

In relation to military problems, the special senses present an interesting hierarchy among themselves that constitutes a commentary on the nature of warfare, particularly modern warfare. The special senses are the mechanisms by which the body is informed of its external environment. The military importance of a sense is directly proportional to its range, that is, primarily to the distance at which it yields information, and secondarily to the variety and precision of that information. In this hierarchy vision is king. It is our exteroceptor *par excellence*. Hearing stands next, while all of the others are of relatively minor importance. This rank order of importance is demonstrated by the number of investigations of military significance that have been undertaken at the request or suggestion of one or another branch of the Armed Forces, and it is reflected again in the list of topics that will be dealt with in the present Symposium.

The importance of vision is obvious. No other sense gives us direct personal information as to the presence of objects or the occurrence of events at so great a distance. It also allows us to determine the direction of distant objects with accuracy and to aim our weapons accordingly. The great power of visual discrimination, whether of form, of brightness, or of color, requires no elaboration. The practical importance of adequate vision in military operations is indirectly attested by the defensive measures taken to avoid visual recognition, such as smoke-screens, camouflage and the blackout. Furthermore, for most of us vision is the dominant sense in our mental processes. Man is a visual animal and in case of conflict of various forms of sensory evidence, vision usually is the one upon which we rely. In some individuals auditory imagery and auditory memory may be equally important with the visual, but for almost all of us "seeing is believing".

Hearing gives us the possibility of rapid and accurate communication by means of language. It makes possible the speedy reception of information from other men, and when its range is increased by instruments, such as the telephone and radio, it assumes a position of great importance. The information is usually secondhand in that it generally consists of what some one else has seen or what a

superior officer wishes us to do. Hearing is indispensable, but only under special conditions does it become the primary sense that makes contact with the enemy. The distances over which hearing, unaided by instruments, is useful is shorter than the range of vision, but hearing has the advantage that it is available at all times. It is as good by night as by day and it is the sense which remains most active during sleep. Our sense of direction by hearing is relatively poor, but as a general warning, whether arousing us from sleep or attracting our attention while awake, hearing is "the watchdog of the senses". It is an interesting commentary on the relative importance of vision and hearing that the phrase "watchdog" comes naturally to mind. The word "watchdog" is anthropomorphic. A watchdog really does not watch. He is a "hark-dog" who relies more on his ears than on his eyes.

The ear is not hampered by natural obstacles such as night and fog, but under conditions of modern warfare it frequently is forced to operate under "smoke-screen" conditions of our own making, as in the noise of an airplane, a tank or an engine room. We shall see that the problem of maintaining communication in an atmosphere of noise of our creation is one of the chief military problems of hearing.

Another exteroceptor is the sense of smell. We can distinguish and, particularly with training, can recognize a great variety of odors; but smelling is biologically a lost art. If we were dealing with the military problems of dogs we should probably have a large chapter on problems related to the sense of smell; but apart from possible questions of nuisance value or of recognition of special substances, such as poison gas, for which neither vision nor hearing are adequate, it is difficult to imagine many serious military problems involving the sense of smell.

The sense of equilibrium and of orientation with respect to gravity is an exteroceptor to a very limited degree inasmuch as it gives an orientation with relation to our surroundings. The tactile and proprioceptive sense that enables the aviator to "fly by the seat of his pants" might be mentioned for the sake of completeness, but it scarcely presents special problems. Abnormal functioning or irritation of the labyrinth may be very distressing, as in the case of motion sickness, and the problem of the proper discounting of false impressions of position and rotation during aerobatics is one of interest and significance. The range of information yielded by the labyrinth is limited, however, and the military importance of this sense organ hinges chiefly on its nuisance value.

When we reach the senses of taste, touch, pain and temperature we have come to such close quarters that the problems become almost too personal to be of major military significance. The importance of these senses from the military point of view has shifted from a dependence on the sense for obtaining useful information to one of avoidance of discomfort and distraction. In other words, their chief importance is their potential nuisance value.

We have already indicated two of the major types of problem that arise in relation to the special senses: First the protection and, by implication, also the possible improvement of a necessary function. The second is the avoidance of personal distress or discomfort, as from extremes of temperature, unpleasant smells or tastes, the itch of skin irritations, the pain of wounds, or the nausea and disability of motion sickness. We shall have little to say about any of the latter class of problems. The approaches to them are fairly obvious. One possibility is to attack the very obvious cause of the discomfort. Another is to allay the distress by the use of drugs, but in few instances are the special physiological properties of the sense organs very clearly involved. The soldier is expected to endure considerable discomfort, but when it becomes so severe as to impair his efficiency the solution is usually sought in some practical compromise aimed at reducing the stress to which he is exposed.

The possible improvement of vision and of hearing is a fascinating thought, but we already know that we cannot expect much in this direction. Good normal ears and eyes function about as well as it is possible for an eye or an ear to perform. We are limited by the nature of the structure of the eye and the ear and also by the nature of light and of sound. A very few photons arriving at the retina suffice to produce vision in a fully dark-adapted eye. The ear is sensitive to movement and pressure changes in the air at an energy level only slightly above that of the thermal agitation of the molecules. The real problem is to preserve at its best efficiency the sensitivity which nature has already given us. How can we best protect our eyes and ears against fatigue and against the loss of sensitivity resulting from unfavorable general conditions, such as malnutrition or anoxia? What are the possibilities of failure from temporary overload, such as we find in aviator's deafness or in snow blindness? One of the important military problems of the special senses is to determine with some accuracy the limits of tolerance of vision and of hearing under extreme conditions of severe stimulation and to devise methods of protection and conservation.

The problem of dark adaptation of the eye is a special one with which we are all more or less familiar and which will be dealt with specifically by one of our contributors. Fortunately there is no corresponding problem in the case of hearing unless we include in this comparison the temporary deafness

that results from exposure to very loud noises. No time-consuming process of adaptation is normally required to re-adjust the sensitivity of the ear to enable it to hear faint sounds following exposure to any sound that can properly be considered within natural limits.

Problems of interference with function by unwanted but unavoidable competing stimuli are rather similar for both sight and hearing. The glare of sunlight or of searchlights may prevent us from using our eyes to their normal advantage. The aviator's tactics of approaching his enemy "out of the sun" is a familiar illustration of this principle. Nature provides few sounds loud and continuous enough to mask hearing as effectively as the direct glare of sunlight dazzles vision, but man-made noises within planes and tanks form a serious obstacle to communication even when they are below the level that may cause temporary loss of hearing. The problem of minimizing these difficulties by proper aeronautical design is considered specifically in one of the contributions to our Symposium.

Although we cannot hope to improve significantly upon the performance of the best eyes and the best ears, there is, nevertheless, a great difference in performance between the best eyes and the worst eyes and between good ears and bad ears. We are all familiar of course with the frequent rejections of men from military service because of faulty eyesight and, less frequently, because of deafness. The problem of selection of personnel with respect to special abilities and disabilities of sight and hearing is an important one. Not only do we find nearsightedness, farsightedness and astigmatism, which may be corrected by glasses, but there are also the special disabilities of color-blindness, and, more rarely, night-blindness. Deafness may depend upon faulty transmission of sound to the inner ear resulting from old infections of the middle ear, or there may be a deficiency of the sense organ itself either as the result of disease or from previous exposure to very severe noise. It is being recognized more and more clearly that at least two standards should be set up with regard to sight and hearing. First, a minimum standard, representing the worst performance that is compatible with active military duty, and secondly, special criteria for special assignments. It is obvious that good eyesight is more important for an aviator than for a member of the Quartermaster Corps. While extreme acuity of hearing is of little significance in a tank it may be all-important in an outpost or when listening for enemy airplanes or submarines. It is also becoming increasingly apparent that mere acuity of hearing or sharpness of vision or a high degree of dark adaptation does not tell the whole story. There are also more subtle faculties of the central nervous system that enable one man to understand speech in noisy surroundings better than his fellow or to recognize the significance of and interpret correctly what he sees. These more subtle and complex functions rest upon native ability, but they may also be improved by training. The selection and training of personnel for specialized assignments is one of the important military problems of the special senses.

RED GOGGLES FOR PRODUCING DARK ADAPTATION

WALTER R. MILES

Laboratory of Physiological Psychology, Yale University School of Medicine

Effective vision at night or in darkened rooms depends upon adaptive processes in the eye whereby the receptor mechanisms, cones and rods, become increasingly sensitive for a period of one half hour or more. In the past, the potential observer has had to wait in the dark until he could see. The amount of this waiting time to achieve something near maximum sensitivity of the eye was about 30 min. in complete darkness. The adaptation time required to reach a certain threshold level is lengthened if the subject has previously been in very bright light, or it is shortened if the previous environment has been of a relatively low brightness level. The effects of brilliant, glaring environment can be reduced by the use of proper goggles, and ordinary indoor working light can be made very dim by such means. Through use of the goggle method the eyes are thus partially adapted before being introduced to the real darkness, and the period required in the dark is shortened. For several years x-ray operators have used such goggles as a means of preparing their eyes for fluoroscopic work. The goggles were worn for several minutes while engaging in ordinary office work before going to the darkroom and during intermissions when the operator wished to leave the darkroom. In this way, quite a saving in time is achieved. Neutral, green, and red goggles, in general of rather high density, have been available for these x-ray purposes, and such equipment has also been used by various industrial workers preparing for darkroom activity.

vant data have been discarded, and the results show a good degree of consistency.

Threshold values procured after using the red goggles without the subjects having been light adapted (lines shown in dots and dashes) tend to be slightly lower than when wearing of the goggles was preceded by light adaptation. This result was to be expected, since the brightness level of the laboratory rooms was considerably below that of the light adapting screen.

It was not expected that thresholds following light adaptation and the red goggles would be quite as low as with light adaptation and darkness. The red filters pass some light that stimulates some of the rods because a fair amount of perifoveal vision is present when one is wearing the goggles.

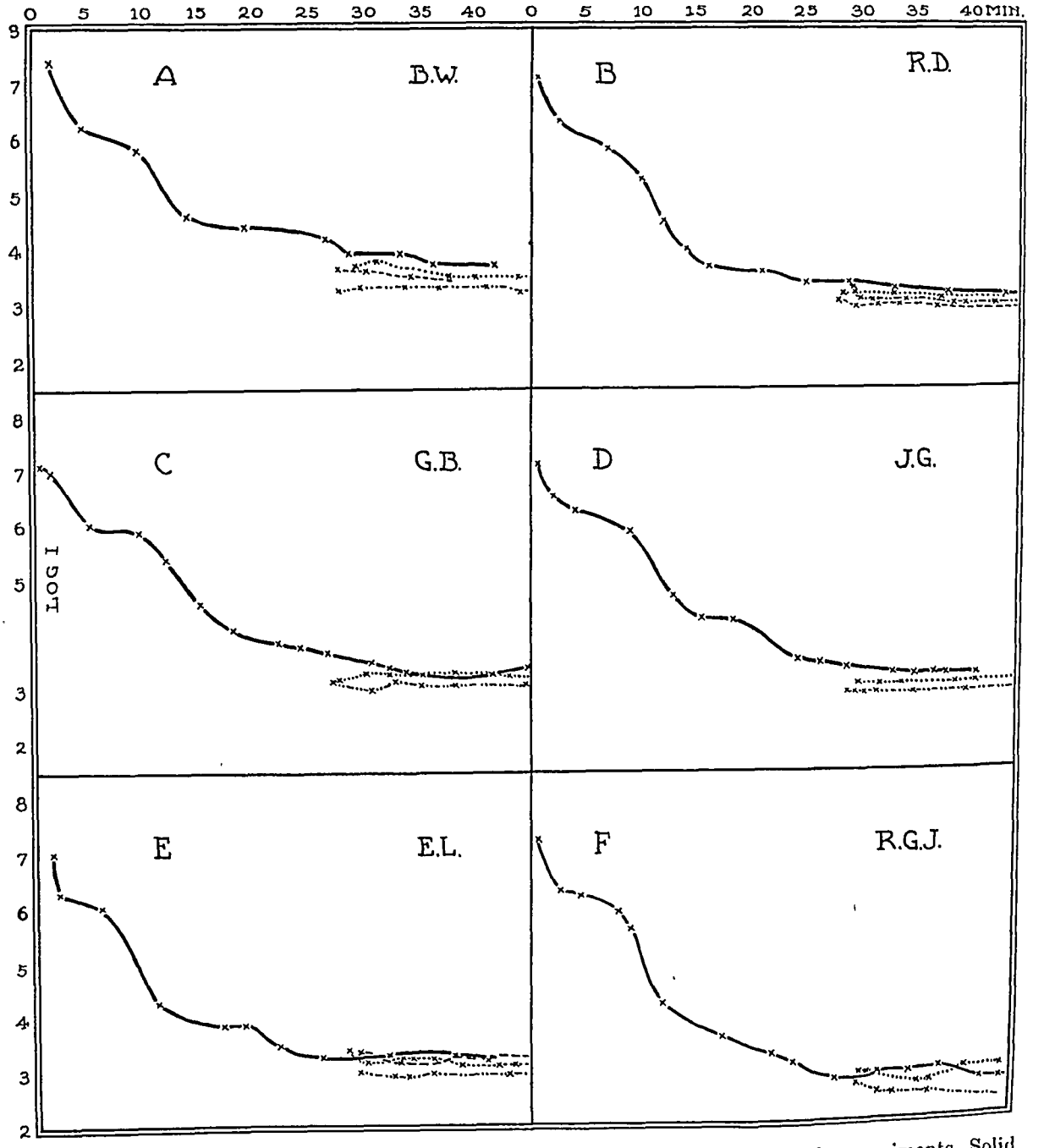

Fig. 2. Comparison of dark adaptation thresholds for goggle and non-goggle experiments. Solid line curves represent thresholds taken in darkness following standard light adaptation. Curves plotted in dots or in dashes represent thresholds after standard light adaptation and after wearing the red goggle in a lighted room for 25 min. Curves shown in dots and dashes represent thresholds after wearing the red goggles for 25 min. but without previous standard light adaptation.

The apparent advantage of securing a lowered threshold by the goggles may be an artifact caused by retinal fatigue or by general fatigue. The experiments carried out with the goggles made somewhat less demand on the subjects than when serving for the full adaptation curve. Also, the portion of retina tested in the experiments was subjected to more low level stimulation for obtaining the thresholds represented in the complete curve than in the goggle tests.

An experimental procedure was tried with the red goggles that approximated more closely that of the regular experiment in darkness. Preadaptation to light was used, then the subjects remained in the adaptometer room, put on the goggles, and the ceiling light was turned on. The subject looked at magazines and conversed with the operator for 4 or 5 min., then the ceiling light was extinguished, the goggles pushed up, and a threshold determination made. The goggles were pulled down, the lights turned on again. In this manner, red goggles with the room light on were used for periods of 4 or 5 min., interspersing the measurements for outlining the complete adaptation curve. Comparative results of this character are shown in figure 3 which embodies the charts of three subjects. The time intervals during which the goggles were worn have been set off with vertical lines, and each such period is marked with the letter R. In the intervening periods the room light was turned off, the goggles displaced from in front of the eyes, and threshold measurements taken. These points are represented by bold solid dots with short segments of curve attached.

In each of the three cases the bold sketched curve tends to fall below the subject's comparison curve or curves made in darkness without the use of the red goggles. In chart I the two curves are near together during the first 15 min., but after that are separated by 0.4 to 0.6 log units. Chart H includes two comparison curves made in darkness. In the interval 20–40 min. following light adaptation both comparison curves are above that for the goggle experiment. In chart G the subject appears to have gotten more rapid dark adaptation with the goggles, but the terminal thresholds are only slightly lower than those found in the comparison test.

Chart G includes an additional broken curve at the top which is nearly horizontal and at a level typical of cone adaptation. This curve is for red stimulus light secured by using a Wratten 88 filter in the adaptometer in place of the Corning 5113. It is a simple matter to shift these filters and thus record curves for violet stimulation and red stimulation during the same experiment. The two threshold determinations for red made within the first 10 min. are 0.2 to 0.3 log units lower than those found later in the goggle experiment on this subject. The intermittent wearing of the red goggles thus decreases the sensitivity of the cones for the red stimulus in the adaptometer test patch. This

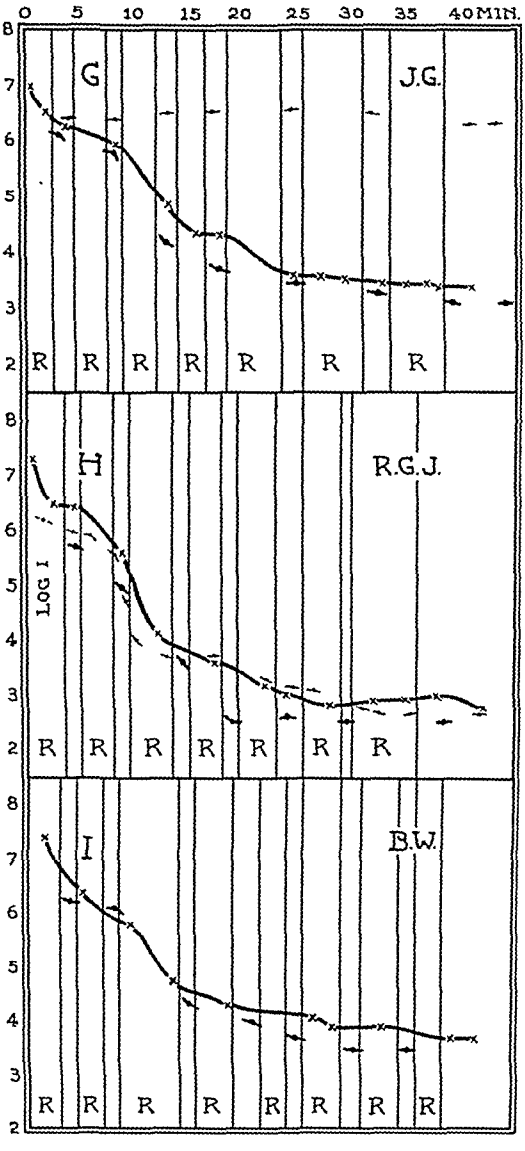

Fig. 3. Dark adaptation curves with and without red goggles. The broken curve composed of bold dots shows thresholds when red goggles were worn intermittently in a lighted room. Solid line curves represent thresholds during adaptation to darkness.

is a result which would be expected. That the rise in the curve is no greater than shown is probably in part due to the fact that the red goggles were not

worn continuously. Whenever the room light was turned off the cones would begin recovering from their red adaptation.

Discussion. The tests reported here on the effectiveness of red goggles for achieving dark adaptation were all conducted between October 16 and November 19, 1941, in New Haven. Prior to this a single pair of goggles as described above had been put together for trial. Following the tests 12 pairs were made according to the same specifications, and these were distributed to organizations and individuals interested. The data presented show good consistency and essential equivalence of brightness thresholds for the regular dark adaptation method and for the red goggle method.

As a first approximation based on the photopic and scotopic visibility curves for red light the filter chosen for the experimental red goggle proved to be usable and effective. However, its transmission was relatively low.[5] It seemed probable that a filter with a cutoff at 600 mμ might be adequate for the purpose. Later experiments by others have proved this to be the case (4) (5). From the results here presented it seems obvious that dark adaptation essentially equivalent to that secured by waiting in darkness for 25 min. can be achieved by use of various red filters chosen in relation to the illumination level of the room or area in which the adaptation period is to be spent by the personnel interested. This is not the place or the time to discuss such details or routines in reference to exact duration of periods of wearing the goggles and of being in darkness before beginning the different types of work involving night vision.

These experiments clearly demonstrated that the routine of waiting in the dark to accustom the eyes to their night duty tasks was quite unnecessary. That rather dreary procedure can be avoided and the time that it requires occupied in more cheerful and more useful pursuits. Personnel preparing for night duty by wearing dark adaptor goggles desire to have as much useful vision as possible. Therefore, for general purposes it seems unnecessary to use a red goggle that has a density that tends to adapt the eye to a level lower than it would naturally adapt to in, for example, a starlit area. Practical considerations must govern the goggle specifications and routines suited for military operational or industrial needs.

The results of these experiments are not sufficiently extensive to lend themselves well to statistical treatment. However, so far as they go, they consistently indicate that red light enhances the rate of the adaptation processes in the retina beyond that which normally takes place in the presence of darkness. So far as the writer is aware, this is a new finding. Its explanation is not at present clear, and it obviously calls for more detailed and critical experimentation.

Summary. 1. Goggles for reducing the light and partially adapting the eye to darkness have been routinely used by x-ray operators and industrial workers. The usefulness of such goggles for securing complete dark adaptation was here made the subject of experimentation.

2. Specifications were based on the photopic and scotopic visibility curves in the red and an experimental goggle employing Corning filter No. 2403, which passes no visible radiation shorter than 620 mμ, was made and tried out by means of taking dark adaptation thresholds with the Hecht-Schlaer adaptometer with practiced subjects.

3. After light adapting the eye in a standard manner and wearing the red goggles in a lighted room (5 ml.) for 25 min., it was found that the brightness thresholds were as low or lower than when the subjects had been in complete darkness for the entire period.

4. Dark adaptation thresholds made by using the red goggles intermittently showed threshold curves that were as low or lower than those made while the subject was in complete darkness.

5. The experimental results obtained indicate that deep red light has a property of augmenting the rate of dark adaptation of the eyes beyond that provided by complete darkness during the first 25 or 30 min. of adaptation.

6. The red goggle method of adapting the eye for night vision can be substituted for the routine of waiting in darkness and offers the practical advantage that subjects can engage in tasks requiring reasonably good vision during the period of adaptation.

7. The red goggle technique provides a means whereby night or darkroom duties can be interrupted at will by returning to lighted areas without the loss of dark adaptation. Also, by this means dark adaptation gotten during sleep in a darkened area can be saved while passing through lighted areas to the location of the night vision tasks.

8. Details for specifications of dark adaptor goggles, the timing routine for wearing them, and the illumination in the areas where they are worn are practical considerations to be worked out in reference to specific tasks and objectives.

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[5] Photopic transmission 3.80 per cent; scotopic transmission 0.246 per cent. Personal communication from Mr. R. W. Cheshire.

functioning convergence is necessary for effective space perception; and aspect disparity is a necessary condition for stereoscopic vision.

1. *Binocular convergence.* When an object is observed at a great distance, the lines of sight through the centers of the two eyes are parallel. When the object is near at hand, the eyes are turned so as to focus along lines of sight which converge upon the object. Convergence is brought about by the action of the eye muscles in effecting the co-ordinated turning of the two eyes. Because of this action, convergence may serve as a cue in depth perception. A large amount of convergence means an object which is close at hand; a small amount, an object which is farther away. Convergence cues are probably ineffective for objects at distances greater than 20 yards.

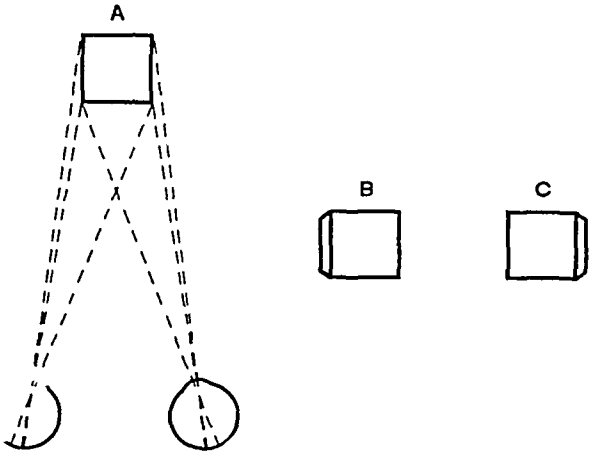


Fig. 1. Examples of aspect disparity. *A* is a view, seen from above, of lines of sight when the eyes look at a solid object. Notice that the right eye sees some of the right hand side of the object, while the left eye sees some of the left hand side. *B* is a front view of a cube seen by the left eye with the right eye closed. *C* is a front view seen by the right eye with the left eye closed. When both eyes are open, we see a fusion of *B* and *C*. This fusion results in the perception of a solid object, the cube, seen in depth.

2. *Aspect disparity, corresponding points, and stereoscopic vision.* When we look at a solid object we do not see the same view with the left eye as we see with the right. This difference in views is called *aspect disparity*. In order for us to perceive depth with maximum effect the two views must be combined. When they are combined, we perceive an object in depth, and this manner of perceiving is called stereoscopic vision.

Figure 1 gives us an example of aspect disparity. The diagram, *A*, represents a top view of the lines of sight occurring when our eyes regard a solid object. Consider what happens when we close one eye, and imagine that the solid object is being regarded from the front as in *B* and *C*. If the right eye be closed, we perceive the view diagrammed in *B*. With the left eye closed we see the object as in *C*. In normal vision, when we regard the object with both eyes, we see it as a fusion of *B* and *C* which represents a solid cube seen in depth. It must be emphasized that if we regard an object with one eye only we see it with a small degree of depth. It is the fusion of the disparate views which produces a maximal effect.

The principle of aspect disparity is used with good effect in the old-fashioned stereoscope. In this instrument the visual field of the right eye is separated from the field of the left eye by means of a partition which extends from the eyepieces nearly to the stereoscope card. The stereoscope card represents two views: the left-hand view photographed from the position of the left eye; the right-hand view, photographed a slight distance to the right from the position of the right eye. These two camera views of the solid object are placed upon the stereoscopic card so that the left-hand view is restricted to the left eye, and the right-hand view to the right eye. In looking at the two views, an observer fuses the two views into a meaningful single view. The fusion is taken to represent a scene which is perceived in depth.

It must be emphasized that stereoscopic vision does not occur under artificial conditions alone. It occurs naturally at any time when we view a solid object in depth. By virtue of the fact that we receive a right eye view and a left eye view of the object, we have a condition for aspect disparity with its consequent stereoscopic perception.

When we are considering stereoscopic fusion for small objects in space it is sometimes convenient to think in terms of correspondence and non-correspondence of retinal points. Stimulation of corresponding points occurs when corresponding parts of retinal images lie on points in the two eyes which are at equal horizontal and vertical distances from the central lines of regard.

Stimulation of non-corresponding points on the temporal-nasal axis of the eyes does not always result in double vision. "Seeing double" occurs only when horizontal disparity exceeds a definite value; below this value, fusion occurs even though stimulation is on non-corresponding points. Within the range of disparity where fusion is tolerated, the perceived distance of the fused object varies with the amount of non-correspondence. As disparity increases, the object is perceived as moving forward or backward in space depending on the direction of disparity.

STEREOSCOPIC RANGE FINDING (3, 4). *The instrument.* There are a number of interesting modifications of the stereoscope. From the point of view of the military man, the most important of

these is the stereoscopic range or height finder. The range finder is a modification of the telestereoscope, the principle of which is represented in figure 2.

In this instrument an exaggeration of the normal depth effect is accomplished by providing mirrors

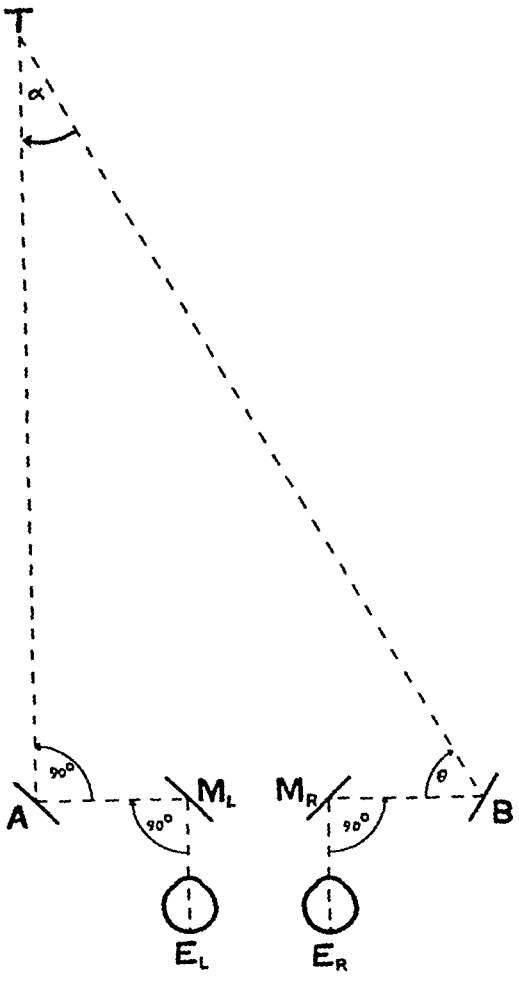


Fig. 2. The principle of the telestereoscope and the range finder. (When the range finder is used for finding the height of planes, it is called the height finder.) The target, T, is viewed by the eyes, E_R and E_L, through the parts of the optical system indicated in the diagram.

at A, B, M_L and M_R. With the mirrors in place, the left eye, E_L, seems to be viewing the object from position A while the right eye, E_R, seems to see it from B. By this means, the angle ATB between the lines of sight for the two eyes is greatly increased over what it could be with naked vision. How much it is increased depends on how long the distance AB is made; and this length in turn determines how much the stereoscopic depth effect will be increased. If the length is increased sufficiently, even targets at great distances yield disparate images to the two eyes and are seen in the third dimension.

The telestereoscope of figure 2 may be converted into a stereoscopic range finder by the addition of two important features. First, eyepiece and objective lenses are inserted in the instrument, and these magnify the appearance of the target as well as enhance the depth effect. Secondly, an artificial field of reference marks, called a reticle, is placed in each side of the instrument, in the space between the two mirrors. As with the two views on a stereoscopic card, the two reticles are seen as one fused image. Some of the marks on the two reticles are alike, but other marks are slightly disparate so that they seem nearer or farther away than the rest of the marks.

When the range finder is directed at a target, T, the target image appears within the reticle field. If the angle θ is varied by turning the mirror B, the target seems to approach or recede with respect to the reticle marks, depending on which way the mirror is turned. It is therefore possible to find a certain value of θ where the target seems to be at the same distance in space as one of the reference marks (usually the center mark) in the reticle field.

In practice, it is just as convenient and more accurate to measure the complement of θ, $90° - \theta$, which is equal to α. Then $\frac{AB}{AT} = \tan \alpha$. But α is a small angle, and $\tan \alpha$ may be taken equal to angle α expressed in radians: $\frac{AB}{AT} = \alpha$. Since one radian equals about 206,000 seconds, $\alpha = \frac{206{,}000AB}{AT}$ or $AT = \frac{206{,}000AB}{\alpha}$ in seconds of arc. When magnification occurs in the range finder, the magnification, M, multiplies the right-hand side of the preceding equation. The resulting equation is

$$R = \frac{206{,}000bM}{\alpha},$$

where b is the base length of the range finder ($= AB$) and R the range ($= AT$), measured in the same units.

The rotational movement of the mirror B may be calibrated in numbers proportional to reciprocals of α in such a way that each determination of α means a certain range from the range finder to the target, base length and magnification remaining constant. Because of the stereoscopic

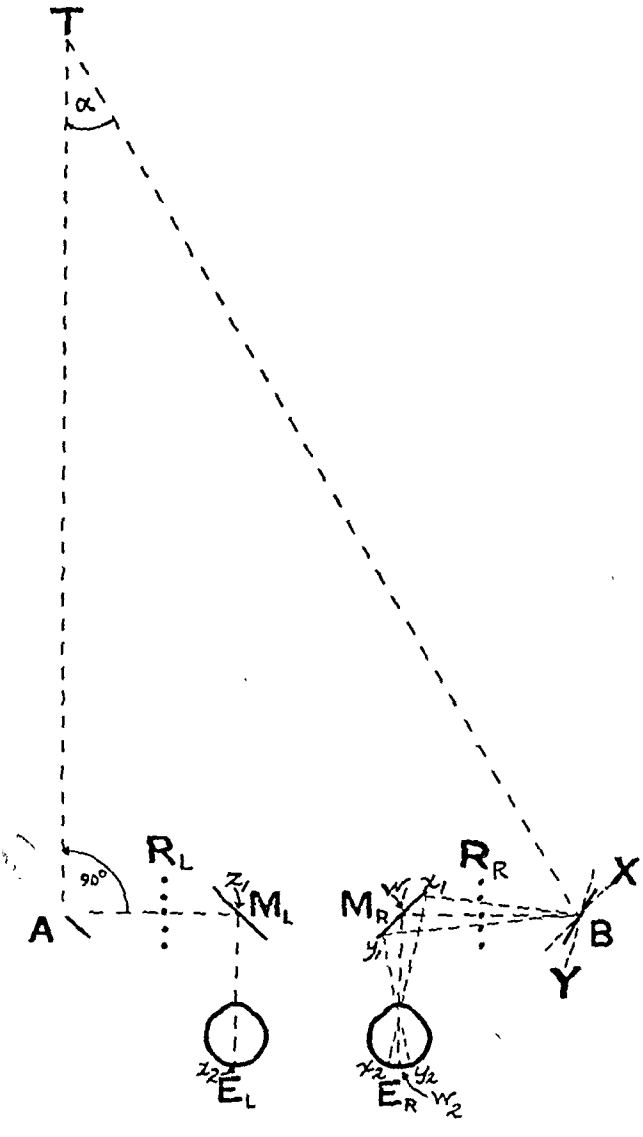


Fig. 3. Stereoscopic vision in the range finder. Explanation in the first footnote.

depth of the target in the reticle field, the observer is able to take ranges with great accuracy.[1]

[1] It is clear in figure 2 that the accuracy with which range can be determined depends upon the accuracy of measurement of angle α. In order to make the determination of α as precise as possible, use is made of the stereoscopic acuity of the observer.

Rays of light from T in figure 3 impinge upon mirror B which is set at such an angle that the rays strike mirror M_R at w_1 and are reflected into the eye, E_R, to w_2. w_2 has a position in E_R corresponding to z_2, a point of stimulation in E_L arising from ray z_1z_2; that is, w_2 and z_2 are corresponding points. (Objective lenses necessary to image T at R_L and R_R are not shown, nor are necessary reversing lenses and eyepiece lenses.)

R_L and R_R indicate reticle lines placed in the optical system. These lines, when regarded through the proper system of eyepiece lenses, are fused, and the observer sees a series of "posts" hanging in space. The central point of each of these reticles lies in the same axis, perpendicular to the page, as the ray from target T. In consequence the perception given by stimulation of points z_2 and w_2 in the two eyes is one of judging the reticle to be above or below T but in the same stereoscopic plane as T.

Consider what happens if mirror B is rotated to X or Y. If the mirror is in position X, rays from the target T follow the path indicated by x_1x_2. x_2 is a point which does not correspond to z_2. Therefore, target T is seen behind the reticle. With the mirror in position Y, rays follow the path y_1y_2 and the target is seen in front of the reticle.

If the optical system is carefully constructed so that positions of R_L and R_R are known, the fused reticle presents a series of lines representing a known distance geometrically. Movements of mirror B required to bring a target into the same plane as the reticle can be calibrated to indicate ranges of targets when the targets are "lined up" with the reticle. Because of the fact that stereoscopic judgment is so sensitive, the determination of angle α can be determined very accurately by this method.

The above description of the stereoscopic range finder is correct in principle but is oversimplified and schematized. In the actual instrument the mirrors are replaced by reflecting prisms all of which are stationary. The variation of θ is achieved by the use of refracting prisms located between B and M_R. These prisms are controlled by the range knob, and the range in yards is read directly from the dial connected with the prisms.

In height finding, the stereo observer depends on two *trackers* to help him keep the plane in view. One tracker mans a telescope at one end of the range finder and the other looks through a telescope at the other end. One tracker moves the instrument in azimuth until the plane appears centered in his telescope; the other moves it in elevation until the plane appears centered for him. When the plane is centered in both telescopes, height readings may be made by the stereo observer.

The stereo observer may follow the plane continuously by attempting to keep the image constantly over the reticle, or he may make separate settings at five to ten second intervals while the plane remains in view. In either case, the settings eventually arrive at the computing instruments which cause the guns to "lead" the plane and to fire with fuses timed to explode near the plane.

The man. The skill of the stereo operator depends among other things on his stereoscopic

acuity. Stereoscopic acuity is the least difference in angles formed by lines of sight to two objects when an observer can just perceive that one of the objects is farther away than the other. This difference in angles is called stereoscopic parallax which is illustrated in figure 4. The parallactic angle in figure 4 is $\alpha_1 - \alpha_2$ for lines of sight formed at objects T_1 and T_2. When $\alpha_1 - \alpha_2$ reaches a minimal threshold value for space perception, the difference is called η. η is a measure of stereoscopic acuity; low values of η mean good acuity; high values, poor acuity.[2]

Under certain special conditions (stationary objects, optimal illumination, etc.) extremely good observers can discriminate angular differences as small as 4 seconds of arc. This figure means that at 100 yards the observer can detect a difference in distance between two objects, lying close together, of about 3 yards. At 200 yards the required difference is 12 yards. When observations are made by following moving objects, judgments are not so good as this. In range finding the angular difference may rise to as high as 45 seconds with a poor operator.

Stereoscopic acuity is important in range finding because it determines the error of ranging. Let us consider the case of the man regarding the two objects, one at 100 yards and the other at 103 yards. If the man can *just* appreciate the difference of 3 yards, he obviously cannot certainly perceive the difference when it is reduced to 1 yard. In other words, if he observes one object lying at 100 yards and the other at 101 yards, he will tend to judge the objects to be at the same distance, and this judgment will be in error by 1 yard.

The same situation applies in the range finder. Even though the operator judges the target and reticle to be "lined up" at the same distance, his judgment may err by an amount which is determined by his stereoscopic acuity. Obviously, an operator with good stereoscopic acuity will make a smaller error than one with poor acuity. The importance of stereoscopic acuity is shown by the fact that an error of 28 seconds in one type of range finder leads to an error of 90 yards in ranging on a plane flying at a height of 6,000 yards.[3]

It is clearly to the interest of the Services that stereo operators be chosen with great care. Men with poor stereoscopic vision will probably never become proficient range finders. Up to the present, a number of devices have been developed for selecting stereo operators with good stereoscopic acuity. Selective methods of this sort are valuable, and they should be used fully for selecting the best talent. In range and height finding only the best talent is good enough.[4]

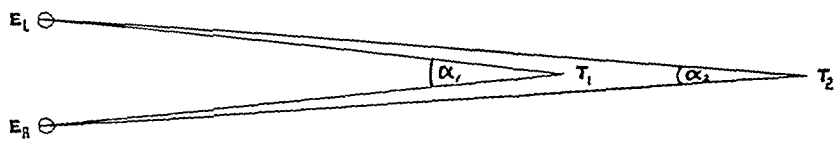


Fig. 4. Parallax in the observation of two objects. The diagram also indicates the influence of increasing base length in the range finder. α_1 and α_2 increase as E_L and E_R are, in effect, more widely separated.

COINCIDENCE RANGE FINDING (3). The coincidence range finder operator makes observations with one eye. Figure 5 shows the principle of the instrument. (Eyepiece and objective lenses are omitted.) Rays of light from target T are reflected from mirrors A and B, rays from mirror A being reflected into the eye, E, by mirror M_L, and rays from mirror B by M_R. M_L is a mirror whose reflections fill only half of the visual field seen by E, e.g., the lower half. M_R provides rays which fill the other half of the field, e.g., the upper half. As the observer looks into the total field provided,

[2] Let d be the distance to T_1 along a line perpendicular to a line, a, joining the centers of the two eyes (the interocular distance). If T_2 lies near T_1 and nearly on the same line perpendicular to a, the distance to T_2 may be called $d \pm \delta$, where δ is the difference in distance between T_1 and T_2 and where δ is small in relation to d. The binocular parallax $\alpha_1 - \alpha_2$, is given by the expression:

$$\frac{206{,}000a\delta}{d^2}$$

in seconds of arc, approximately. At threshold, this is equal to η.

[3] The error, $d\alpha$, in determination of α (figure 2) is related to the error, dR, from the true range, R, by the following equation, where M is the magnification and b the base length:

$$dR = \frac{R^2 d\alpha}{206{,}000bM}.$$

[4] See Ballard (1) for a discussion of certain problems concerned with stereoscopic and coincidence range finding.

he sees a field which is bisected by a fine horizontal line. The subject's task is to adjust mirror B to give an accurate measure of angle α. This is done when mirror B is so adjusted that the two halves of the target complete an unbroken configuration. Proper range is determined when the target has the appearance illustrated in figure 6A.

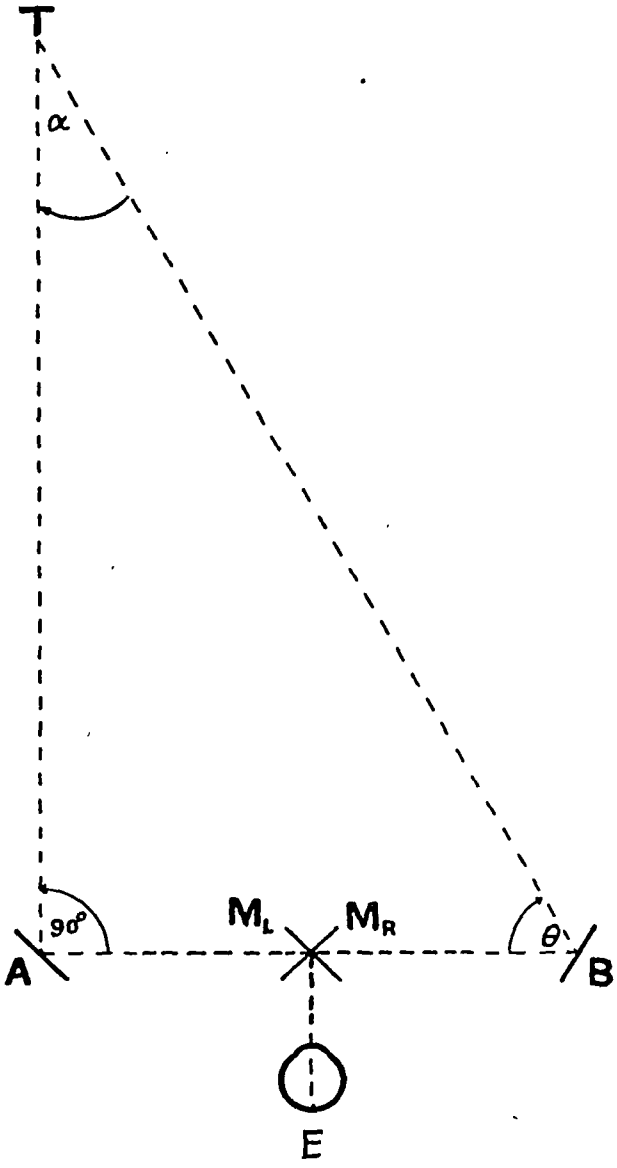


Fig. 5. The principle of the coincidence range finder. M_R reflects rays from B into the eye, E, and M_L rays from A. M_R is placed above M_L in the visual field.

Incorrect ranging results in the effect illustrated in figure 6B.

It is clear that the accuracy of the determination of angle α in the coincidence range finder is determined by the observer's coincidence acuity. Good subjects can make settings, under optimal conditions, with an error of 4 seconds of arc or less.

Equations for range and range error are similar to those holding for the stereoscopic range finder. The coincidence range finder has the disadvantage that, with moving targets, it is difficult to keep the target on the bisecting hairline of the field.

"BREAKING" CAMOUFLAGE (5). Stereophotography usually involves the successive photographing of a given scene from different positions in the air. The resulting photographs are then paired and viewed through a stereoscope. Due to the resulting disparities, the three dimensional characteristics of the photographed objects appear clearly. This method is particularly good for revealing camouflaged military installations, for example, those which have been painted over with drab colors. Since aspect disparity is stronger than any monocular cue, the monocular characteristics (misleading light and shade patterns) of the scene are suppressed and the true spatial characters of the objects are perceived, poorly disguised by the drab coloration.

Stereophotography is sometimes valuable in "breaking" other types of camouflage. For example, if a house or a town be painted on an airport, the deception becomes obvious when a lack of relief appears in the stereophotographs.

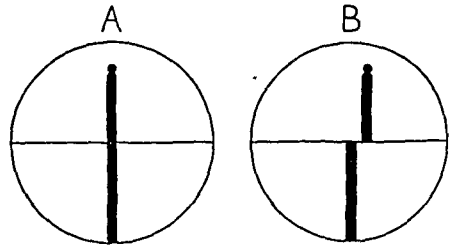


Fig. 6. *A*. View of a flagpole seen in a coincidence range finder when correct range is made. *B*. Incorrect range.

Infra-red photography is another method which has been proved valuable in "breaking" camouflage. The effects of light and shadow can be studied in detail on the film without reference to color. Shadows, buildings, trees, roads, or anything which might be painted on the ground can be examined in the photographs to see whether their appearances "make sense." In order to meet the challenge of infra-red photography, camoufleurs have paid less attention to colors and more to "contour" and "texture" in creating misleading cues. For this reason infra-red photography is faced with more difficult problems, and more and more of the burden of "breaking" camouflage is falling on the shoulders of stereophotography.

AVIATION. It seems likely that most pilots depend to a large extent upon binocular vision in flying. Nevertheless, it is true that an experienced pilot may continue to make good landings even with one eye covered. In other words, stereoscopic vision may be used under ordinary circumstances,

but in extraordinary circumstances the pilot can depend upon other methods. In addition, there seems to be little doubt that some one-eyed pilots have flown successfully for years and certainly without benefit of stereoscopic vision.

A superficial interpretation of these facts might lead to the inference that stereoscopic vision is not necessary to the pilot. However, it must be pointed out that no satisfactory answer has been given on the question of how one-eyed pilots, as contrasted with normal pilots, stand up to the visual strains associated with fatigue and low oxygen. Supporters of present standards are confident that the one-eyed pilot's space perception will fail under stress before the normal pilot's; hence, they recommend that the requirement be maintained.

It may be that binocular vision is not important to the pilot at high altitudes except in formation flying. In formation flying, the pilot must judge and maintain his distance from neighboring planes, and under these circumstances good stereoscopic vision seems important.

Relative motion is a factor that can operate for one-eyed as well as two-eyed pilots and may constitute an important aid to landing. As the pilot lands he perceives the motion of the environment in relation to his head and eyes. Far-off objects are interpreted as distant because they are seen to move *with* the plane and head. Nearby objects seem to *move* against the plane and head. The significance of this space cue to the pilot has not been clearly demonstrated.

A pilot's space perception is a complex and shifting affair. The cues impinging on him at any time are the result of hundreds of variables: the terrain, atmospheric conditions, the particular operation, the particular type of plane, and many others. In these ever changing circumstances, the pilot, like all human beings, makes use of what the psychologist calls the "constancy" organization of space perception.

The term "perceptual constancy" describes the fact that a man can often recognize objects even though few specific cues are presented. A lack in one cue may be made up by the presence of other, even incomplete, cues.[5] In consequence of this, a human being exhibits a learned or innate perception which remains relatively constant in the face of wide variations in data from the external world. "Perceptual constancy" plays an important part in such complicated activities of the pilot as "visualizing the route" and "keeping a sense of direction." In these activities space behavior remains "constant" even when ground patterns, atmospheric conditions, instrument readings and a thousand and one other factors vary.

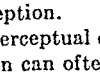
The topic of "constancy" has many implications for the flyer, and we should be in better position than we are to utilize its principles. It seems fairly certain that individuals vary in their "constancy" judgments and that these judgments can be improved by practice.

PERCEPTION OF MOVEMENT AND SPEED (2). The factor of movement increases the complexity of space cues and sometimes provides its own special effect upon the observer. The most refined measurements of movement are made with instruments, but more commonly position and speed are predicted by quick "natural" judgment on the part of a man. The anti-aircraft gunner, for example, predicts and compensates for the speed of an approaching, low flying plane by "leading the target."

Observation of movement is difficult when there is a narrowly restricted background such as occurs when observations are made by searchlight illumination or through a telescope. The difficulty arises because we normally judge the motion of objects by reference to stationary objects in the background. The worst condition of observation occurs when the background is obscured, as it is on a dark night or a foggy day.

Speeds which are too low (less than 3 min. per sec.) or too high (more than 45° per sec.) cannot be observed by the *stationary* eye. It is only in the middle range between these extremes that judgments are reasonably good. These figures emphasize the importance of distance between the observer and the object by calling attention to the visual angle of movement. A plane, flying at 300 miles an hour is at best a blur to an observer at a distance of 100 yards. However, a plane moving at this speed can easily be observed at a distance of a mile. This factor undoubtedly contributes to the great surprise advantage of low flying planes.

Sometimes the eyes of the observer remain stationary while an image of the object moves across the two eyes. More often the observer follows the object with his eyes and keeps the image centered within the region of clearest vision. In the latter case, judgments of motion are based on an appreciation of the relative motion of objects plus a perception of eye and head movements.

[5] A simple case of visual "perceptual constancy" arises in reading words printed in "Shadow" American display type. For example, readers have little difficulty in understanding the word "Of" when they see  . This is true even though the merest outlines of letters are presented. It is tempting to relate this type of activity to those conditioned responses which are founded on complex stimuli, but which are later elicitable when only one member of the complex is presented.

Fatigue, alcohol, low oxygen, and unbalanced eye muscles are among the common hindrances to coordinated pursuit of an object by the two eyes.

It is certain that we have no special sense for perceiving speed and direction. Instead we must use our eyes and muscles in an appropriate way and learn to put together the messages which result from this behavior. This skill is unconsciously developed in different degrees by different individuals. It is so specific that a person who is good at following a moving target may be poor at estimating the speed of his own vehicle.

Under certain conditions, "illusions" of motion can be obtained from stationary objects, e.g., moving pictures. Certain types of "animated" electric sign also provide this effect. If light from one bulb in the sign goes on and off rapidly and is ollowed within a short period of time by light in fanother, the resulting perception is one of movement, that is, the observer sees movement from the first bulb to the second. This effect is the phi phenomenon of the psychologist. If enough bulbs are provided, a complex scene may be "animated" by this method.

Another illusion of movement, important to the soldier, is encountered in "tracer cutback," When an anti-aircraft machine gunner fires at a moving airplane, his tracer stream seems to bent more and more as it gets closer and closer to the plane. In effect it develops a "shoulder" away from the plane or a "hook" toward the plane. There is some physical basis for this marked effect, since it can be shown that the apparent tracer stream lies along a slight curve. However, the curved appearance is greatly exaggerated and cannot be accounted for on a strictly physical basis. It is probable that movement effects provide the illusory accentuation of path curvature. "Tracer cutback" causes considerable difficulty for inexperienced gunners and it may seriously reduce the accuracy of fire.

No general rule can be given for the improvement of conditions for the observation of movement. Each particular situation must be analyzed for itself and many of these situations are so important that careful analyses are needed. The observer should be thoroughly trained in the particular kind of judgment which is required, and experienced and apt men should be used wherever possible.

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THE EFFECT OF ANOXIA ON SENSE ORGANS

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Early observations made during expeditions to high altitudes called attention to the effect of lowered barometric pressure on mental activity and sensory function. They were the starting point of quantitive experiments performed either at high altitude, in the low pressure chamber, or in experiments involving the inhalation of oxygen-nitrogen mixtures. Since no essential differences resulted when the effect of a lowered barometric pressure was compared with that of a reduction in oxygen tension at normal barometric pressure (1) the results seemed to be due to the lowering of the oxygen tension only.

The greater part of the work has been performed on optical functions. It has been shown that the threshold for light is raised under conditions of light and dark adaptation (2-6). In these, as well as in other investigations, the effect increases with decreasing oxygen tension in the inhaled air. It is worthy of note that a measurable dimunition in sensitivity is noticeable when subjects are exposed to a simulated altitude of only 7400 feet (McFarland and Evans.) The threshold for discrimination of light intensities increases also (7, 8). Experiments on visual acuity show a de-

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cisive loss of this function under conditions in which discrimination of visual intensities is involved (9). More recent studies of McFarland and Halperin (10) emphasize, however, that the effect on visual acuity is a function of the light intensity used in the experiments. They find that at low intensities the visual acuity is greatly decreased under conditions of anoxia whereas at high intensities the effect is slight. The study of visual after-images reveals decisive changes on inhalation of oxygen-nitrogen gas mixtures (11) as well as in the low pressure chamber (12). The latent period of negative after-images increases, their intensity becomes apparently greatly diminished and in some instances they may be suppressed completely. All effects are reversible on inhalation of air.

The effect of anoxia on the peripheral field is somewhat controversial. Whereas some authors (13, 14) believe to have shown a decrease in the visual field in anoxia, others (15) attribute these changes not to an impairment in visual function but to a weakness of attention. The central field of vision appears to be altered by an enlargement of angioscotomata (16). It is probable that these changes are only in part due to alterations in the size of the retinal blood vessels (Cusick, Benson and Boothby, 17) and reflect largely alterations in the functions of the ganglia of the retina (Evans and McFarland, 16). Widening of the blind spot has also been observed in anoxia (13). Investigations on color vision in the low pressure chamber seem to indicate that this function is likewise diminished. Velhagen (18) reports a diminution in color sensitivity at a simulated altitude of as little as 3000 m. Schmidt (19) confirms these results but emphasizes in contrast to Velhagen that the different types of color blindness, although aggravated, persist in anoxia and cannot be transformed by anoxia into another type.

It is of interest to note that on recompression visual functions may be increased temporarily above the normal level. Schubert (7) states that recompression is accompanied by photisms and an increased sensitivity to intensity discrimination. It is worthy of note that on recompression to 5000 m, the visual discrimination of intensities may be better than normal when this altitude is reached from 7000 m, although it is decidedly subnormal when this level is reached on decompression. Anoxia lowers the critical fusion frequency (C.F.F.) for both direct and indirect vision (Seitz, 20).

The sensory preceptions involved in the performance of active movements are likewise impaired. McFarland, Knehr and Berens (21) show a diminished degree of coordination of reading movements in anoxia. Kostitsch (22) describes experiments in which the subject performs two similar movements with a Mosso ergograph. He observes that the movements become increasingly dissimilar at a simulated altitude of 5000 m, or at 6000 m in the case of altitude-resistant individuals. Since these movements are performed with great accuracy even against varying loads and with anesthetized fingers (De Rochemont, 23) probably Golgi-Mazzoni corpuscles in the connective tissues surrounding the muscles play an important part (von Frey, 24).

No detailed investigations have been reported on the influence of anoxia on vestibular sensations, although Ruff and Strughold (25) mention that they likewise decline in sensitivity. Gellhorn and Spiesman (26) show that vestibular reflexes in men measured by the number of nystagmic movements following caloric stimulation are altered to a lesser degree than sensory functions such as hearing and vision. They find that inhalation of 10 per cent oxygen from 7 to 50 minutes causes a decrease in the nystagmic response only in some of their subjects.

No quantitive investigations on the effect of anoxia on taste and smell have been published although Hingston (27) reports a diminution of taste sensations and inability to taste onions and peppermint at an altitude of 16,500 feet.

Gellhorn and Spiesman (28) find the hearing threshold to rise when 9 to 12 per cent oxygen was inhaled for 8 to 30 minutes. A slight improvement in hearing is observed temporarily when 12 to 15 per cent oxygen is used. Lowering of the barometric pressure causes the upper limit of hearing to decrease by 1100 to 4900 vibrations per second (Hartman, 29). No effects of anoxia are seen up to a simulated altitude of 4000 m. These values have been obtained by using bone conduction in order to eliminate the effect of lowered barometric pressure on the middle ear. When pure oxygen is inhaled at lowered barometric pressures the upper limit of hearing remains unchanged.

Reduction in barometric pressure diminishes the sensitivity of the pressure receptors in the skin. This phenomenon has been observed above 7000 m during the Himalaya expedition on acclimated persons by Hartmann (30) whereas Strughold (31) notes a similar increase in the threshold at 5500 m in the low-pressure chamber.

Although it is obvious from these data that sensory functions decline in anoxia, the question as to whether this is due to a diminution in the function of the sensory structures involved or secondary to changes in attention and cooperation has not been studied adequately. Kyrieleis and Siegert (15) explain the fact that in their investigations no changes of the peripheral visual field occur in the low-pressure chamber by their method through which they exclude as much as possible the factor of fatigue. They are inclined to interpret

the positive data of earlier investigators by "Aufmerksamkeitsschwäche." However, it is to be remembered that a decrease in various sensory functions has been observed at relatively low altitudes with trained observers which makes such an interpretation unlikely. Moreover, the simultaneous study of critical fusion frequency (C.F.F.) and brain potentials (electroencephalogram, E.E.G.) demonstrates parallel changes in subjective (C.F.F.) and objective (E.E.G.) phenomena during anoxia (36) (fig. 1). If, due to unusual resistance to anoxia no changes in C.F.F. occur during the inhalation of 7.8 to 8.4 per cent oxygen the appearance of the E.E.G. as well as the reactivity of the alpha waves to light remains unchanged.

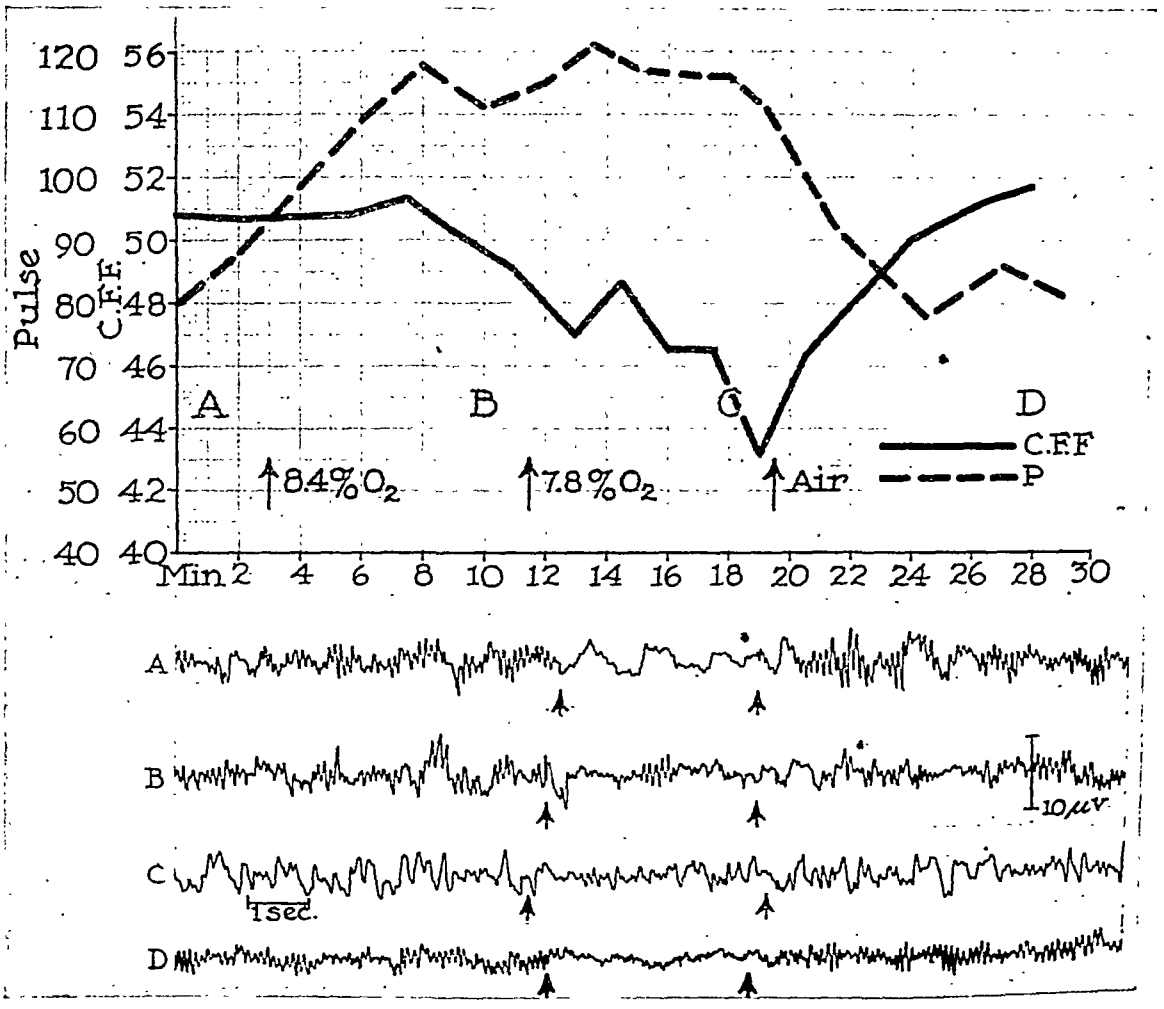

Fig. 1

The fact that cutaneous and proprioceptive sensations may be impaired in anoxia although the sense organs involved will not be injured by relatively long periods of depletion of their blood supply proves that in this case the effect of anoxia must be central rather than peripheral. The situation is somewhat different with regard to the visual system because the retina is composed of a complex set of ganglion cells whose metabolism is not essentially different from that found in other parts of the central nervous system. This is illustrated by the fact that hypoglycemia and anoxia act synergistically on the visual threshold of the dark adapted eye (32) and on the electroencephalogram (33).

Anoxia could act on this system in one or more of three ways by affecting 1, photochemical processes in the retina; 2, retinal synapses, and 3, the geniculate-striate system. The rapid recovery of the light sensitivity of the dark adapted eye following readmission of air seems to indicate that the effect of oxygen deprivation on visual function is extraphotochemical (4, 5). Craik's (34) demonstration that local pressure, while rendering the eye blind, does not prevent the formation of after images when the pressure is removed also proves that anoxia acts on the retinal neurons and not on the photochemical system. More direct evidence for the role of the retinal neurons in anoxia is found in the work of Seitz (20) and Seitz and Rosenthal

(35). These authors show that local application of strychnine to one eye counteracts the effects of anoxia without interfering with the action of anoxia on the other eye. Thus they observe that the strychnine treated eye regains a normal C.F.F. and normal angioscotomata during anoxia whereas the untreated eye shows the characteristic fall in C.F.F. and an enlargement in the size of the angioscotomata. These investigations suggest that the retinal synapses are more sensitive to anoxia than are those located in the geniculo-striate system. It should, however, be remembered that the final sensation and perception is certainly greatly influenced by the reactivity of cortical neurons.

Simultaneous recordings (36) of C.F.F. and E.E.G. (fig. 1) illustrate the interaction of peripheral and central factors. It is found that with the beginning of the fall in the C.F.F. during the early stages of anoxia as illustrated in record B there is a diminution of the effect of vision on the alpha waves before any change in the E.E.G. is noticeable. In the middle of the period of object fixation a series of alpha waves of unchanged amplitude appears which are absent at this period in records A and D taken before and after the anoxia respectively. This record also shows that the E.E.G. is still normal; later most of the alpha waves were replaced by delta waves (cf. part C of the E.E.G.).

These data suggest that anoxia impairs visual processes through interference with the transmission of nervous impulses from the retina to the brain as well as through alterations in cortical functions.

Further advance in the understanding of retino-cortical relations under conditions of anoxia is to be expected from simultaneous recordings of retino- and electroencephalograms.[2]

The effects of anoxia on sensory functions are minimized through respiratory, circulatory and neuro-endocrine adjustment reactions (38). Acclimated persons show lesser changes in pulse rate and sensory function under conditions of reduced oxygen tension (30). Autonomic reactions leading to pupillary dilatation (39) and retraction of the nictitating membrane (40) tend to offset the effects of anoxia on vision. However, the effects on circulation and respiration are of far greater importance as illustrated by the fact that inhalation of 3 per cent carbon dioxide may offset the effects of 8 per cent oxygen on visual intensity discrimination (41).

In this connection the fact that retinal and cerebral circulation follow similar rules is of interest (42).

SUMMARY. Lowering of the oxygen tension impairs the function of the sense organs, the critical level being dependent on the degree of acclimatization. Anoxia acts largely through its effect on the synaptic nervous system of retina and brain. The parallelism between subjective (sensory) changes and alterations in brain potentials indicates that the former are based on functional changes of the retino-geniculate-striate system. In the case of non-visual functions such as perception of pressure and movements anoxia is believed to act on the central nervous system only, particularly on the cortex since subcortical reflexes are less sensitive to anoxia than are sensory functions.

[2] Riggs (37) has described a method for obtaining a retinogram in man.

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Fig. 1. Effect of inhalation of 8.4 to 7.8 per cent oxygen (between the arrows) on pulse rate (----), critical fusion frequency, (——) and electroencephalogram. The E.E.G. records marked A, B, C and D were taken at the time indicated by these letters on the graph. Between the arrows marked on the E.E.G. the subject opened the eyes and fixated an object.

VISION, HEARING AND AERONAUTICAL DESIGN[1]

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It is principally through the sense of vision that pilots are aware of the nature of terrains, weather conditions, the terrestrial orientation of their aircraft, and the position and movements of enemy planes. Even so-called "blind flying" is primarily a visual function. Here the "contact" is transferred from the horizon and ground objects to the special instruments upon the panel. Hearing likewise is of critical importance to military flyers in that command information and assistance from ground control stations must be audible over the communication system. Also intercommunication systems within aircraft must function as the principal means of maintaining prompt and coordinated action of members of air crews in carrying out military missions effectively. These facts are generally known and accepted by plane designers. However, engineering success in providing for ease of seeing and ease of hearing is quite variable, and these basic pilot requirements merit our continued attention.

Take for example the almost complete blanking off from vision of an area directly ahead of the pilot when a plane changes its normal flight attitude to a landing attitude. This is particularly vicious in the case of fighter aircraft with large air-cooled engines in the nose of the ship; and the condition has resulted in a great number of avoidable landing, taxiing, and take-off accidents. Aircraft carrier accidents have undoubtedly resulted from this blanked off area, in spite of the fact that a landing signal officer is supposed to direct the landing properly. Mirror reflections of the area immediately ahead of the plane could be provided. Tricycle landing gear on some few aircraft have done much to benefit this blindness due to radical change in plane attitude.

Engineers are no doubt aware of the desirability of placing pilots, observers and gunners as near as possible to the transparent panels through which they must get their visual impressions. The nearer the eye is to the window, the larger the visual field that can be seen through it, or for a given angular field, the smaller the window needed. The ordinary spectacle lens 1½ inches in diameter gives the wearer an uninterrupted view of almost 90°. Close proximity to airplane windows also makes for clear visual fields: (1) it is easier to provide the requisite transparent area free from obstructing pillars, panel joints, and opaque accessories; (2) marks, specks, and scratches on the window surfaces are less bothersome because they are out of focus, and (3) when near the window, the observer's head makes an area of shadow which is helpful, particularly at night, since it blocks off reflections from the inner surface.

THE GUNNER'S VISUAL PROBLEM. The position of gunners in relation to windows is especially worthy of consideration. We may take a hypothetical set of measurements for discussion. The gunner's eye must be about 9 inches behind the gun sight; the sight is 20 inches from the aiming panel; the gunner's seat is therefore placed against the back wall of the turret, and the space in front of him is well filled with gun supporting and operating structures. The aiming panel is a beauti-

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fully clear, optically perfect surface 14 x 14 inches. The engineers are to be congratulated on this window, but not on the position of the gunner. For him the situation resembles that met in tunnel vision. His eyes are 29 inches away from this superb window which can provide him with a view of only 28°, that is 28° of the full 60° to 90° that are so critically needed.

The aiming panel must of course be well mounted, and this calls for a rather heavy metal frame. Sometimes it is as much as 2 inches wide. Other small, usually curved windows border the aiming panel, and each of these must have or share a frame with adjoining windows or wall structures. When the guns are in front of the gunner, sections of the mounting structure, brackets, electrical switches, etc., frequently have locations which obscure portions of the windows from the gunner's eyes. The total effect is a lattice window with the lattice predominating over the clear space in some instances. From the gunner's view through a particular panel, a total of only 25 per cent is unobstructed to binocular vision; 53 per cent is totally obstructed; 22 per cent is obstructed for one eye. Juliet could manage to get an eye full of Romeo through a lattice window, but our gunner is not cast in the role of a shy lover. For him the irregular lattice is a hazard to vision and life. It is true enough that through the lattice he can see a lot of landscape as he looks from one opening to another. What he needs to see, however, is moving planes. When his eyes catch sight of one, they try to follow it. This is done by a special kind of coordination in the action of eye muscles and is known as pursuit eye movement. The eye actively glides along at a rate set by the visual target and appropriate to keep it in clearest possible view on the fovea. Visibility of the moving target is essential for this type of seeing. Whenever the moving target momentarily disappears, as happens when it passes behind opaque lattice areas, the pursuit movement is immediately stopped. The eye jumps to the far edge of the obstruction and waits. When the target emerges, a new pursuit movement must be organized by the nervous system. This necessarily costs an average delay of .15 of a precious second before clear pursuit vision can be reestablished. The gunner is of course not completely blind during this interval, but his visual efficiency on the moving target is hampered by every opaque gap across which he is compelled to operate.

In turrets where the guns may be mounted at the sides and rather low down, it should be possible to reduce the amount of structure in front of the gunner and to bring him forward much nearer the front panel. This will increase his angle of uninterrupted view, make visual pursuit of his targets easier, and reduce the blinding effect from the flashes of his own guns.

VISION INSIDE THE COCKPIT. Inside the cockpit we usually observe a confusing multiplicity of instruments and the lack of a suitable grouping of essential flying instruments according to a well planned pattern for visual perception. For purposes of night flying where visual function is largely dependent upon maintenance of dark-adaptation of the eye, instrument panels in general are subject to the following serious faults:

1. There is too large an illuminated area. Instruments which are referred to infrequently are constantly illuminated.

2. The color of the transmitter or reflected light from these instruments is usually not of the spectral band least disturbing to night vision, and

3. Intensity as well as total area of illumination is considerably too high. This is usually a criticism equally applicable to direct or indirect lighting, radio-luminous, or fluorescent marked instruments. The only light which can be controlled easily both as to spectral character and brightness level is indirect red light. The use of a spectral red whose transmission band lies in the region of 600 millimicrons is recommended for instrument lighting. The intensity of such light may be permitted to vary considerably without adverse effect upon night vision.

Transparent cockpit enclosures, although of fairly clear optical plastic, discolor with exposure to sunlight; some of them become finely checked due to temperature changes and vibration. Nearly all of them are capable of being scratched too easily, and the result is interference with vision. Measurements of visibility through plastic windows, compared with bullet-proof glass and with open cockpit view, show that the glass produces a slight loss and that the loss from the plastic may be 5 or 6 times as much. Flat panes consistently provide better visibility than do curved plastic surfaces, but they may also give an increased drag. A compromise must be made between visibility and aerodynamic considerations. Rapid strides in development of better plastics are being made, and it should be possible soon to mold transparent cockpit enclosures of better grades of optical plastics in one piece. Surface hardening of such molded parts is desirable. Close attention should be given to reducing inside reflections which are particularly troublesome from concave surfaces.

In military aircraft we often find that vision forward and to either side is fairly well provided for but that even though the pilot may have the usual well developed rubber neck, he is handicapped by certain design features of his plane in seeing what may be above or aft. It is often forgotten that in actual combat pilots refuse to leave the "green-

house" closed and must therefore use goggles. Any fixed aperture made available for the pilot's face should not be too small to permit use by a bespectacled or goggled aviator.

AIRSICKNESS AND VISION. Airsickness of passengers and crew may result from unavoidable motion stimulation of the vestibular mechanism of the ear, from rapidly changing gravitational forces acting on viscera, muscles, and joints, and from apprehension and past unhappy memories of plane travel. All of these upsetting stimuli are as a rule less disturbing if those affected can see out and establish visual contact with the horizon, with cloud formations, and with the ground scene below. We should remember the old instructions to novices in flying, "Never look at the up wing; watch the down wing." Many troop-carrying glider craft afford virtually no opportunity to look out and establish visual contact beyond the plane. To arrive at the scene of battle with a load of thoroughly ill troops contributes nothing to fighting morale and effectiveness. A part of the answer to this difficulty is—don't require passengers and crew to fly blind.

HEARING SUFFERS MORE THAN SIGHT. The ears more than the eyes are subjected to environmental stress through flying. It seems to be true of modern aviation that every time the engineers increase the power and speed of our airplanes, the ears of the pilots take a greater beating. Although the ear is a magnificent little mechanism—the most intricate mechanical structure in the human body—it is a rather delicate device and one which seems ill designed for modern war. But the ear has gone to war, along with the rest of the soldier, and we are compelled to admire the service it renders in the face of acoustic stress.

Airplanes have always been noisy, and they are becoming noisier. A thousand horsepower fed into a propellor is able to agitate the atmosphere in a thunderous manner, and when the engine delivers two thousand horsepower the din is doubled, or actually more than doubled, because as the tip speed of the propellor increases a larger proportion of its driving energy is converted into sound. When this energy pounds on the ear, it is striking a mechanism so sensitive that less than one quintillionth of a horsepower is needed to produce a faint sensation of hearing. In addition, more horsepower means more speed and hence more turbulence about the ship. It is this turbulence of the slip stream over the wings and about the fuselage that produces the distressing, high-frequency random noises which sound like a mighty "shhhhhh." In some respects the noise from the turbulence about the plane is more of a problem than is the noise from the propellor itself. This is demonstrated in planes which do not have propellors. Contrary to popular notions, the interior of a glider plane moving at about 150 miles per hour is a very noisy place. The noise level is about 115 decibels, and conversation in such a place is difficult, if not impossible.

In any really fast moving vehicle the noise is random, that is to say, all frequencies of the spectrum are present. When we listen on the ground to a plane high overhead we hear only the low frequencies of the propellor. But inside the plane it is different; there we hear all frequencies added together at once, producing a noise which is to sound what white light is to light. And as a general rule, the greater the speed, the "whiter" the noise. Also as a general rule, the whiter the noise, the more objectionable it is to the ear. White noise is objectionable for three reasons: (1) it is disagreeable, (2) it produces temporary deafness, and (3) it spoils communications.

That white noise is annoying needs little argument. No one has been found who really enjoys it. It is true, however, that our attempts to prove that long exposure to intense airplane noise is damaging to human efficiency have produced essentially negative results. When adequately motivated, a man can code a message, add columns of figures, coordinate his movements, react to a signal, etc., about as well after 8 hours in a noise of 115 decibels as after a similar period in the quiet. Despite this remarkable experimental result, our subjects all report that they find the noise unpleasant, and they are happy when it is turned off.

TEMPORARY DEAFNESS. That airplane noise produces deafness is a well known fact. In normal ears this deafness shows two characteristics: it is restricted more or less to the high frequencies, and fortunately, it is usually temporary. After 8 hours in an airplane noise of 115 decibels, the normal ear shows a hearing loss of about 40 decibels in the region of 4000 cycles. It has sometimes been supposed that low-frequency airplane noise produces high-frequency hearing loss. On the contrary, it is the high-frequency components of the noise that produce the high-frequency loss. The ear, for some unknown reason, is more vulnerable at these high frequencies.

Recovery from a 40-decibel hearing loss usually occurs in about 24 hours. The recovery is rapid at first and then proceeds more slowly. About half of the loss is regained by a normal ear in the first 3 hours after exposure. Some ears apparently do not have this power of recovery, and repeated exposure to noise leaves them permanently deafened. Although we usually blame the noise for such deafness, there is a question as to whether the ear itself is not the real culprit. At any rate, many ears appear to develop high-frequency deafness without excessive exposure to intense noise.

IMPROVEMENT OF COMMUNICATIONS. The most

important practical effect of airplane noise is the masking of communications. Not only is conversation impossible in some planes, but even over radio and interphone speech signals are often masked beyond recognition. Articulation tests have shown that with much of our standard military interphone equipment a listener is able to understand only about 50 per cent of the words spoken in the presence of an airplane noise of 120 decibels. Over the same interphones more than 95 per cent of the words are understood when there is no ambient noise present to interfere with the speech.

The difficulty of communicating under the handicap of airplane noise calls for vigorous remedies. Constructive measures can be applied in three general directions.

First, the plane can be quieted to some extent, either by improved aeronautical design or by the application of sound absorbent materials. Acoustic treatment that is light enough to be tolerated in a plane does not appreciably reduce the overall noise level. It does, however, change the spectrum of the noise by reducing the intensity of the high-frequency components. Hence, the noise in an acoustically treated plane is less "white" and therefore less bothersome than the noise in an untreated plane. Tests have shown that, for the same overall sound intensity, conversation person-to-person is relatively easy in a treated plane but quite impossible in an untreated one.

The second remedy calls for an improvement in the response characteristics of the communication equipment itself, especially of the microphones and earphones. A loud noise does not interfere with intelligibility nearly so much when instruments of high fidelity are used. But with microphones that have non-linear distortion and with earphones that at some frequencies are sharply resonant, the effect of an airplane noise of 120 decibels is to reduce the intelligibility of speech by 30 to 40 per cent. High-fidelity equipment is not yet being widely used in airplanes, although a few major improvements are now in process. Complete overall high fidelity from microphone to earphone must be achieved if speech is to be transmitted to and from our most modern airplanes.

The third remedy called for by the noise problem is the shielding of the microphone and the earphones from the noise. The oxygen mask could be so designed as to shield the microphone from the ambient racket, but many otherwise excellent masks suffer from acoustic defects. This problem is now under study, and improved noise shields for hand-held microphones are being developed. The earphones and the ear of the listener can be shielded from the airplane noise by means of an acoustic socket designed to provide a tight seal against the side of the head. In present military equipment this provision has been neglected, but improved devices are now in production. Some of these ear protectors serve to reduce the unwanted sound in the aviator's ear by 20 to 50 decibels.

Conclusions. In general, it can be said that the problems raised by intense ambient noise are serious but not insoluble. Judicious use of sound treatment in the plane, conversion to high-fidelity microphones and earphones, and the development of acoustic devices to shield the mouth and the ears of the personnel will permit the aviator to carry on in the best noises which the aeronautical engineers are now planning to produce.

The flying and efficient fighting of modern planes is largely dependent on the special sense of vision. The eyes fortunately suffer no great decrement in function from the swift movement or high and changing elevation of the airplane. Vision is adequate to the basic task assigned to flying personnel. The chief difficulty is in providing for optimal visibility through the structures of the plane and for continuous visual check on the environment surrounding it in both day and night flying. Ideal visual conditions are not wholly attainable because of aerodynamic and structural necessities. However, we should make the effort to gain all possible visual advantages. The problem is a continuing one and offers important strategic possibilities.

Both seeing and hearing, if accompanied by prolonged attentive effort, especially under conditions of unfavorable plane design, are capable of contributing to pilot and air crew fatigue and loss of efficiency. It has been proved worthwhile to give the airplane engine an adequate combustive mixture by supercharging and to pay special attention to protecting the oil in the engine against "foaming" at high altitudes and reduced barometric pressures. It is proving and will prove worthwhile to consider the flyer's eyes and ears and the rest of his very mortal body and to reduce in every possible way the tendency to physiologic and psychologic "foaming" in him.

BRITISH PHYSIOLOGY AND THE WAR

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For some years before the outbreak of War people in Britain could see the shadows darkening and the dangers approaching nearer. From 1933 onwards a constant stream of displaced scientists from Nazi Germany sought sanctuary and opportunities to continue their useful activities in Britain.

The Society for the Protection of Science and Learning and the related American bodies did much to salvage this talent; British physiology was enriched and stimulated by the addition to its ranks of men of the caliber of Feldberg, Ellinger, Krebs and many others. Those who attended the last International Congress at Zurich in 1938 must have felt the imminence of crisis. The opening addresses were devoted to reaffirmation of such elementary principles as the rights of the individual and the international fellowship of science.

There was considerable tension at the meeting of physiologists who had recently been driven out of Germany and Austria, and those who had supplanted them in their posts. It was only a month or two before Munich and the destruction of Czechoslovakia. Many of us as we talked to our Czech colleagues had grave fears for their future; before long we knew what their fate was to be.

With the coming of war an official policy of partial evacuation was decided upon and all persons and institutions whose services could be dispensed with were advised to move to safer areas. Acting on these instructions the University of London had arranged to move all its constituent schools, including of course its Medical Schools like University College, Guy's, St. Thomas', St. Bartholomew's, St. Mary's, the London Hospital and the London School of Medicine for Women.

These schools are responsible for the training of nearly as many students as all the English provincial medical schools taken together. Each School was left to make its own arrangements to transfer to an appropriate center outside London. In view of subsequent events it is rather ironical to recall the evacuation areas which were chosen. Many of the supposed "cities of refuge" like Bristol, Manchester, Glasgow and Birmingham, were later heavily bombed and suffered as much or more than London itself. Some of the schools were more fortunate, like the London and St. Bartholomew's who went to Cambridge, or Guy's who organized an entirely new medical school for themselves in the country.

On the outbreak of War the pre-clinical departments of the London Medical Schools moved according to plan. The difficulties associated with evacuation at that time can be well imagined. Two important research centers became immediate and complete casualties. A. V. Hill found himself with his laboratory of nerve-muscle physiology closed, his apparatus removed and his staff completely dispersed. The many American physiologists who have enjoyed Hill's hospitality and have had the advantage of his direction in research will deeply regret that circumstances have dealt so hardly with this famous laboratory.

Fortunately Hill's colleagues—Parkinson, Downing, Katz and Schmitt—have all been directly harnessed to the war effort. Hill is very modest in describing his own present activities; he says "I am myself employed wholly on work which I would not be doing if it were not for the war." Americans will, however, recall the period he spent in Washington as Air Attache, and no doubt know that he is an influential Member of Parliament who is doing much in the highest quarters to encourage the fullest use of British scientific personnel.

The other laboratory to disappear was that of John Beattie at the Royal College of Surgeons, where normally a wide variety of problems are vigorously tackled. He began the war with a staff of 15 whole or part-time researchers; within four weeks they were all in the Army, Navy, Air Force, or Women's Auxiliary Services, including Beattie himself who became Colonel, Auxiliary Medical Service.

The laboratory had collaborated in the organization of the Army Blood Transfusion Services and now organized itself as an overseas research unit—stationed in France—for the investigation

of shock. All the equipment was lost during the withdrawal of the B.E.F. in June 1940. O'Shaughnessy was killed on the beaches at Dunkirk. Beattie on his return was seconded temporarily from the Army and was soon at work again till a heavy bomb damaged his laboratories in October 1940. This led to a second short suspension of activity but partly with the help of the Rockefeller Foundation new laboratories were equipped and opened in March 1941 in the country.

To return again to the evacuated London schools in their new homes. The hosts everywhere were most helpful and considerate, but of course difficulties were numerous. To cap everything, Britain was not bombed seriously and by Christmas 1939 many of the evacuees began to feel that they would be more comfortable and just as safe at home. Steadily they began to drift back or planned to do so at an early date. The Women's School that had gone to Aberdeen regarded itself as particularly unfortunate in having chosen one of the very few places where small-scale raids were at that time not uncommon. The medical schools outside London were at this time working quite normally apart from the complications produced by their guests.

No sooner had Britain settled down comfortably to the "sitzkrieg," than France fell, the Battle of Britain was fought and won and the bombing of London, which was to continue for many months, began. You have received full accounts of the heavy loss of life and limb and the serious damage to property that resulted; but it is more difficult to give how readily the work of a great city can be disorganized by more trivial disturbances. The transport problem of London is always a difficult one; the raids did not help it. On arrival at the laboratory there might be no water supply, no gas pressure, little electricity, and the windows blasted with no protection from wind and rain. Attempts at day-time work were often interrupted by "alerts" which necessitated taking shelter. The night raids were very noisy, lasted through the best part of the hours of darkness and were not conducive to study or reflection. All these considerations influenced the London Schools that had returned to move out once more.

The different hospital and medical school buildings in London suffered to a variable extent. The Physiological Department of St. Bartholomew's was destroyed by fire, together with all its research equipment; St. Thomas', University College and Guy's were badly damaged and other places suffered to a lesser degree. St. Mary's alone remained in London carrying on with great fortitude throughout the blitz, and fortunately escaping injury from high explosive.

The experience of University College and St. Thomas' has provided lessons on how to equip an emergency medical school in a hurry. The recipe is as follows: "take a large girl's school in the country, turn the main building into a residential hostel, convert the kitchens into biochemical and histology rooms and turn the stables into experimental laboratories (this is very important); a few old Army huts then serve for Anatomy and other purposes." Following these directions you should be ready to start work in 1 to 3 months.

When the raids spread to the provinces, Bristol, Liverpool, Manchester, Sheffield and Glasgow suffered considerably, but fortunately the attacks on any of these centers were far fewer in number.

The first war duty of the physiological departments was to maintain their teaching services for students. The mistakes made in the last war were recognized and the formal decision was taken that the output of doctors must be maintained to meet the enormous demands of the Services for medical personnel. The departments, in spite of much depleted scientific and technical staffs have carried out their teaching work successfully and the numbers of medical students have been well maintained.

In one large school the professor and senior demonstrator alone carried through a 46 weeks' teaching course in the first 52 weeks of the war; in another school an evacuated professor together with one steward was responsible for all the teaching in experimental physiology, histology, biochemistry and pharmacology, but for one term only. The students have not only worked hard to complete their courses in the minimum time, but have had to devote their little leisure to compulsory military training and civil defense duties; even text-books have often not been available in adequate numbers.

Junior technicians have become increasingly scarce as a result of the call-up and the competition of higher paid posts for juveniles in war industry. Supplies of animals (frogs, cats, rabbits) have been insufficient because of the black-out, the competition of the fur trade and (for rabbits) the food market. On one occasion the American Red Cross collected a large consignment of frogs in Chicago and had them flown to London by R.A.D. Ferry Command.

But in the main all obstacles have been satisfactorily overcome; the combined efforts of teachers and staff have kept up the high pre-war standards of medical education; and students in large numbers are being sent on to their clinical work with a sound technical knowledge and a good grounding in the principles and methods of science.

About 40 physiologists are in the Services, mostly in a medical capacity, but some as combatants; Ludwig of Leeds was killed in action flying for the R.A.F. Five are employed in the civil Emergency Medical Service; Tookey-Kerridge died while acting as Pathologist to an E.M.S. Hospital. Many more are connected with the Blood Transfusion Service organized jointly by the Medical Research Council and the Ministry of Health.

It is more difficult to provide particulars of research activities of physiologists related directly to war problems. They are usually of a secret character (sometimes unnecessarily so) and no details may be published even of the nature of the investigation, much less of the results obtained. It may be stated, however, that there are teams of whole and part-time researchers in a number of institutions engaged on such inquiries. There are a number under the direction of the Medical Research Council of which Sir Edward Mellanby is Secretary. A. N. Drury is dealing with the large-scale preparation of dried plasma, and there has been much published work on changes in stored blood and other matters related to blood transfusion for shock and hemorrhage.

The principal teams to which reference should be made are at the National Institute for Medical Research (until last September under Sir Henry Dale, and since then under his successor C. R. Harrington); at the Research Laboratories attached to the National Hospital for Nervous Diseases (E. A. Carmichael), and the Royal College of Surgeons (John Beattie); at Oxford (E. G. T. Liddell), Edinburgh (I. de Burgh Daly, with the collaboration of members of the Polish Medical Faculty) and University College (F. R. Winton and W. H. Newton).

Sir Joseph Barcroft is head of the Unit of Animal Physiology of the Agricultural Research Council; though the unit is mainly concerned with long range problems connected with ruminant digestion, it also bears in mind opportunities for immediate application of results. Barcroft is also Chairman of the Food Investigation Board which is at the moment concerned chiefly with experimental work in connection with drying of goods for civilian and service purposes.

Information about the activities of individual researchers is difficult to collect, and the details I can quote are undoubtedly incomplete. I have avoided reference to men engaged in studies of nutrition, animal reproduction and biochemistry as these I understand are the subject of special surveys; but I cannot avoid the temptation of mentioning J. C. Drummond whose work as Chief Scientific Advisor to Britain's Ministry of food has been an outstanding success.

Lovatt Evans and Harkness are working for the War Departments; Ing at chemical defense; Solandt is head of a group examining the physiology of men in tanks; Bryan Matthews is in charge of an Air Force laboratory examining the physiology of aviators with the help of Parkinson; Downing is on Air Force instruments; D. K. Hill after a spell as scientific advisor to the C.-in-C. of Anti-Aircraft Command is serving in a similar capacity with the First Army; Andrew Huxley and W. Burns are in Admiralty research parties; and there may be another physiologist going out as Scientific advisor to the Army in India.

To complete the picture I must add that many physiologists hold important appointments in the Home Guard, in Senior Training Corps attached to the Universities and Civil Defense, and on various Government Advisory Committees. Sir Henry Dale as President of the Royal Society is Chairman of the Scientific Committee directly advising the War Cabinet.

A good deal of research is still taking place on fundamental physiological problems, as witnessed by the valuable papers still appearing in the journals, though the bulk of published work has fallen to nearly one-third of pre-war level. Nor have contributions to speculative thought been altogether lacking. Sir Charles Sherrington has crowned a unique career of experimental enquiry by the publication of his Gifford Lectures on "Man on his Nature," which may in the opinion of good judges prove to be the most important philosophical work of the century.

Symposium on Physiological Fitness

PHYSIOLOGICAL FITNESS AND PERFORMANCE—AN INTRODUCTION

MAURICE B. VISSCHER, CHAIRMAN

University of Minnesota, Minneapolis

The fitness of the human organism to perform various tasks is conditioned by both the environment and the state of the organism. The problems involved are extremely complex. Physical and chemical conditions in the environment and in the body are of determining importance. Psychological factors, including especially motivation, play a rôle which under many circumstances is more crucial than changes in physical and chemical conditions. Regardless of whether one agrees that ultimately all physiological mechanisms have their basis in physical and chemical phenomena there is no doubt that at the present time it is expedient to consider these mechanisms at different levels of analysis. Some of the most important psychological factors cannot in general be analyzed profitably in physical or chemical terms at our present state of knowledge.

The state of the body depends upon many remote and immediate factors. Gross changes in the environment must often be considered in conjunction with delicate differences in the ctive state if one is to analyze correctly and ciate reasons for differences in performance. a difference in motivation may mask the effects of large changes in other conditions which might alter performance in one direction or the other without such interference. Likewise the opposite situation has sometimes occurred. For these reasons carefully controlled studies are both unusually difficult and essential.

If an excuse for this Symposium is necessary it is to be had in the urgency of studies upon performance in unusual and unfavorable environmental conditions, and of studies on optimal conditions, both of the organism and its environment, for industrial performance. These objectives are not new to applied physiology but they are made more important by virtue of military needs and the civilian problems resulting from them.

An apology, or better an explanation, is due regarding the incompleteness of the Symposium. Unfortunately two prospective contributors have been prevented, by military duties, from completing their accepted assignments. The remainder of the series of papers is being published, nevertheless, because it is believed that these papers make a significant contribution to a clarification of certain aspects of the problem.

PSYCHOLOGICAL FACTORS IN RELATION TO PERFORMANCE AND FATIGUE

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Problems of performance, particularly industrial performance, have a complex character. The study of labor supply, selection of workers, work methods, energy expenditure and health hazards require the participation of sociologists, psychologists, efficiency engineers, physiologists and physicians. Such interdisciplinary research leads to a creative synthesis—a science of human work.

Unfortunately this cooperative approach is still rather rare in this country. Within the limits of single scientific disciplines significant work has been done on various aspects of human performance. In physiology the studies reviewed by Sacks (31), Gemmill (11), Dill (8, 9), Behnke and Stephenson (2) and the textbooks of Schneider (33) and of McCurdy and Larson (21) illustrate important contributions to the study of human work and physical exercise. The situation is less satisfactory in the industrial field. American psychology has more contact with industrial problems. *The Journal of Applied Psychology* is an important research repository and the Psychological Corporation of New York, collaborating with psychologists throughout the country, provides consultants and research workers for industry (1).

The cooperation of specialists from different fields is exemplified in the work of the Employment Stabilization Research Institute of the University of Minnesota "in which the skills and view points

of the economist, the industrial engineer, the social worker, the medical practitioner and the psychologist were brought to bear upon the conditions and consequences of unemployment" (Paterson and Darley, 25, p. 125).

In Europe the interdisciplinary approach received considerable attention. In France this kind of research centered in Henri Laugier and Bernard Lahy and was reported largely in the journal *Le Travail Humain*. In Great Britain there is the National Institute of Industrial Psychology under H. J. Welch and Charles S. Meyers, and the Industrial Fatigue (Health) Research Board.[1] In Russia organized research was proceeding on a large scale with the Bechterev Institute for Brain Research (Leningrad), the Central Psychophysiological Laboratory (Leningrad), the State Scientific Institute for Economy, Organization and Hygiene of Work (Moscow), and the Institute of the Ukrainian Work Commissariat at Charkov. In Italy there is the Laboratory of A. Gemelli (Milan) and the Centro degli Studi sul Lavoro (Turin), first under A. Gatti and later under Alberto Marzi. Schemes for a large general Institute in Rome got little beyond the construction of a handsome building owing to political intrigues. In Germany the Kaiser Wilhelm Institut für Arbeitsphysiologie (Dortmund) and its journal have been active since the late twenties, and other laboratories like the Institut für Luftfahrtmedizin at Hamburg regularly apply the interdisciplinary approach. Shortly before the outbreak of the present war Japan announced the creation of an ambitious Institute for the Science of Labor.

The purpose of this paper is to point out some psychological aspects of human work and the techniques involved in their study. The treatment is illustrative and limited to industrial examples. More detailed summaries have been prepared by Viteles (38, 39), Jenkins (14), Moore (22) and Tiffin (36). Psychological factors involved in military performance were recently surveyed in a symposium edited by Pratt (28).

I. Psychosomatics. On the purely experimental side much interesting research on psychological factors in performance has been done by French and Russian workers and was summarized by Laugier and Liberson (17).

Liberson investigated the interaction of sensory and motor components in voluntary movements. The subjects were asked to move the index finger as quickly as possible. In the control experiments this was done in the air without contacting any object. In the experimental series the index finger touched a pliable sheet of paper which did not offer any appreciable resistance. Under this arrangement the movement frequency was higher and decrement appeared later. Liberson explains this phenomenon as the effect of a sensorimotor synthesis.

A study by M. Marchae (20) illustrates the participation of visual data in the control of muscular performance. He trained his subjects to lift a weight rhythmically by means of a cord passing across a pulley. In the first half of each experimental period the subjects worked with open eyes and could visually control the length of the displacement. In the second half the work was done with closed eyes. When muscular work was continued for a longer time the lack of visual control was accompanied by work decrement and irregularity in performance.

The effect of mental set on voluntary movement was established in early experimental studies on reaction time. In 1888 Ludwig Lange differentiated between a sensorial and a muscular reaction according to the focus of attention: in sensorial reaction the attention is directed toward the stimulus, in muscular reaction toward the release of motor impulse. In Lange's experiments with sound stimuli sensorial reaction was some 100 milliseconds longer than muscular reaction. In later experimental work the difference obtained was smaller but still persistent. R. S. Woodworth comments that "the muscular attitude is a single-minded readiness to react, while attention to the coming stimulus diverts a fraction of the energy, the size of this fraction varying with the subject's understanding of the instructions" (41, p. 308).

In a different kind of experimental situation, Liberson also demonstrated the effect of mental set on muscular performance. When the subject moves his index finger back and forth the amplitude and the speed differ with the "mental polarization." There are three possibilities: either he conceives of his task as a simple alternation, as repeated flexions, or as extensions of the finger. The results demonstrate a significantly greater efficiency of the "flexion set." Similar results were obtained by Liberson in other muscular movements in which there is possibility of varied "mental polarization": anterior and posterior flexion of the head, closing and opening of the eyes, protrusion and retraction of the tongue. Liberson summarized his data as follows: "These curious facts show that the mental control of the direction of a movement constitutes a fundamental limiting factor when our effort is directed toward a rapid succession of movements" (17, p. 419).

[1] This Board began work during the first World War. Its reports, through 1937, covered the following items: Hours of work and rest pauses (7 reports), dexterity (5), accidents (4), atmospheric conditions (12), vision and lighting (7), vocational guidance and selection (10), methods of work, and monotony (14), posture and physique and machine design (5), miscellaneous, including noise and the menstrual cycle (6).

Physical effort produces an increase in the metabolic processes only partly accounted for by the liberation of energy needed for contraction of muscles which directly take part in a movement. The general augmentation of cellular metabolism seems to be a result of the diffusion of excitation and requires participation of the higher nervous centers. Laugier and Liberson reported relevant experiments undertaken by Russian workers in which use was made of conditioned reflex and of experimental hypnosis. Olnianskaya (24) demonstrated the participation of the central nervous system by using the first technique. Subjects stepped on and off a chair. A metronome indicated the rhythm of work and served as a conditioning stimulus. The daily work period was two minutes; after 10 consecutive periods the subject was exposed to the sound of the metronome but did not do the actual work. Nevertheless, the respiratory exchange did increase during the two minute period of conditioned excitation. This increase was maximal on the first day, decreased rapidly, and disappeared completely in a few days.

Experiments on the effect of conditioning on the heart rate were made by Liberson and Marquès (19). For a number of months a subject was trained to work on a bicycle ergometer peddling without resistance for two minutes after which electromagnetic brakes were applied for five minutes. At the end of the conditioning period the brakes were not applied, yet the heart rate showed the typical increase during the five minute period. The increase was maximal for the first minute and was still perceptible at the fifth minute. During the following five days the average of the five minute readings fell below the normal work level (transitional conditioned inhibition) and gradually returned to normal.

Another Russian worker, Nemzowa, utilized the method of experimental hypnosis. When the experimenter suggested to the subjects, who were in a hypnotic state and performing muscular work, that the work was very hard, the energetic cost increased 15 to 30 per cent above the normal work level. Even more surprising were the effects of the suggestion that the work was much easier than usual: the cost of work decreased as much as 40 per cent below normal.

A survey of American experimental studies on work and work decrement was made by Edward S. Robinson. On the basis of this material Robinson formulated seven fundamental principles of neuromuscular action, over and above the chemical facts of exhaustion and toxicity, which represent laws governing the appearance and progress of objective fatigue. "These principles are not to be thought of as independent of chemical action or as insusceptible to the application of chemical hypothesis. At present, however, our formulation of them is safer if carried out in terms of the *gross* reactions of neuromuscular systems" (30, p. 604). As illustration, the second principle states that the work decrement depends on the amount of repetition and spacing of the specific responses. Homogeneous work such as writing the sequence *ababab* shows a larger decrement in speed than writing the sequence *abcdef* (law of accumulative frequency).

One of the interesting questions related to industrial performance deals with the structure of manual and mechanical ability. Simple observation suggests that motor skill is not a *general factor*, in the statistical sense, a factor which determines an individual's rank in all kinds of *motor performances. For instance, two individuals* receiving an identical amount of training in both operations can be equally good in cementing rubber soles but one might be excellent and the other poor as a stitcher. However, the actual number of *group factors* which determine success in groups of manual operations, and the number of factors specific to particular jobs can be determined only on the basis of experimental and statistical analysis. In an ideal experiment tests measuring various aspects of motor capacity would be given to workers who had received training in a variety of manual tasks. The analysis of the intercorrelations between criteria of proficiency on the jobs and the psychological test scores would indicate the main components of industrial skill.

Willard Harrell (12) administered a large battery of tests to 91 cotton-mill machine fixers and applied factorial analysis to the coefficients of correlation between the scores. The three group factors, components common to a number of tests, were labeled: "manual agility" or manipulative ability; "spatial factor" or the ability to visualize space; and "perceptual factor" or the ability to see details. The manipulative factor was common to tests which required placing pins in a board, and assembling and disassembling nuts and bolts. The spatial factor was important in such tests as the Minnesota paper-and-pencil form board and the punched-holes test. The latter requires visualization of the effect of various ways of folding a sheet of paper on the position of the punched hole. Identification of the third factor was difficult and the label "perceptual" was applied only tentatively.

J. W. Cox (6) in his analysis of manipulative skills identified two group factors: the "mechanical factor" involved in more complicated assembling tests, and the "routine manual" factor common to simple motor tests.

Motor ability is not a unitary trait. Harrell's three common components were narrow group fac-

tors involved in a small number of tasks performed. In other words, "the total number of kinds of mechanical abilities is probably large, and . . . no one factor [ability] is important in very many activities" (12, p. 68).

II. Criteria of efficiency and performance. The final criterion of efficiency is performance in the actual situation. At the laboratory level it is rarely possible to create in entirety the field conditions, and, in any case, it is desirable to use characterizations that have more precise connotation than "good worker" or "battle efficiency." Certain critical aspects of field conditions can be reproduced and functions which are presumably limiting factors are measured. These measurements become standardized laboratory criteria of efficiency. In general, a variety of functions must be measured in a "test battery" and psychological factors should be given a prominent place since these are definitely limiting elements in almost all industrial and military tasks.

In the investigations on the effects of various diets at the Laboratory of Physiological Hygiene, University of Minnesota, psychometric data are used to define the behavioral aspect of the efficiency of the human organism. It might be interesting to survey the techniques which are being used in the current studies on minimum requirements with respect to the vitamin B complex. The "minimum requirement" for a food substance is defined for these purposes as the amount which allows a normal individual to carry on healthy, active, adult life. The "norm" is defined in biochemical (e.g., blood composition), physiological (e.g., heart rate response to standard work) and psychological terms (emotional and social adjustment, psychomotor functions, intellectual level, and retinocortical sensitivity).

The adjustment of the subjects is measured by two techniques: The Minnesota Multiphasic Personality Inventory (13) and a system of rating scales. The basic scale contains 20 items taken from the clinical descriptions of the psychological symptoms accompanying B-complex vitamin deficiencies. This list is used as a self-rating scale and is filled out every other day during the period of drastic restriction in vitamin B intake and twice a week during the period of moderate restriction. A second scale consists of 10 items remaining in the basic list after the subjective items (such as anorexia) were eliminated; this second scale is used in man-to-man ratings once a week. The third scale represents a single weekly composite rating of each subject by each staff member on "cooperation", a term which seemed to summarize best the general character of social adjustment.

The psychomotor tests measure the following aspects of functional efficiency: strength, speed and coordination. Various "dynamometers" belong to the first category. Speed is measured as complex-reaction time involving movement of the whole body; time and accuracy of vertical movements of the forearm combined with pronation and supination of the hand; and velocity of small hand movements (tapping). Path tracing serves as a test of eye-hand coordination. Intelligence is measured by standard tests. The American Council on Education and the Ohio State University psychological examinations, and the Porteus Maze Test (27) are being used. Flicker fusion is a "sensitive test for the excitability of the visual pathways as a whole" (34, p. 252). Obviously other tests might be used in evaluating "efficiency" or "work capacity", but it is believed that the battery does sample the basic components.

In industry output records are used as the yardstick of efficiency. The industrial psychologist also asks what satisfaction and sense of participation the job gives the worker. He realizes that individual maladjustments and dissatisfactions are prone to summate and find expression in the costly form of rapid labor turnover, restriction of output, industrial unrest, and strikes.

III. Job requirements. Job analysis aimed at the establishment of employment standards for the selection of personnel involves description of the task, work conditions, and qualifications of the worker. The latter include: 1, physical characteristics—age, size, eyesight, strength, etc.; 2, experience and training; 3, special abilities, and 4, personality traits.

In an attempt to standardize observations and to pool the findings of different occupational analysts the check-list method was developed. Otto Lipmann used this method in 1916 and his final check list of aspects of work behavior contained over 100 items. Tasks are checked for the importance of each trait and its improvability through training. Two examples follow: "To discriminate exactly at great distances the speed and direction of moving objects, acceleration of movement and diminution of speed"; "To change the nature of the work frequently and to adapt oneself easily each time to the new work" (38, p. 149). The check-list technique was used in a simplified form to develop the Minnesota Occupational Rating Scales (26). This system is useful in selecting personnel with the abilities needed for a given task and in finding the most suitable job for an individual.

Descriptive analysis of job requirements is the basis for the construction of tests by which these abilities can be measured. Where standardized tests are available, a test battery can be assembled. This battery is tried out on workers engaged in the job. Statistical analysis is then applied to

select those tests for a final battery which discriminate between poor and good workers.

The process of developing a test battery can be illustrated from personal experience in the standardization of tests for certain administrative personnel in a large shoe factory. Observation had suggested requirements for general and technical intelligence, clerical ability with emphasis on speed and accuracy, and adaptability to changing tasks. A modification of the Army Alpha test was used as a measure of general intelligence. There were two tests of technical intelligence, one testing spatial judgment and the other consisting of problems in arithmetical reasoning. A shortened form of Thurstone's Examination in clerical proficiency was used, together with a modified Bourdon test and a number cancellation test. These tests were applied to 74 men then engaged on a particular job and to a random sample of other employees of comparable

TABLE 1

Column A: Intercorrelations between the test scores and supervisors' rating.

Column B: Correlation of Army Alpha I.Q. with scores in other tests of the battery.

TEST	A	B
1. Army Alpha I.Q.	0.701	
2. Spatial thinking	0.537	0.597
3. Mathematical reasoning	0.520	0.463
4. Clerical ability	0.387	0.552
Speed (Bourdon)	0.238	0.164
Accuracy (Bourdon)	0.253	0.194
Speed (number cancellation)	0.447	0.297
Accuracy (number cancellation)	0.134	0.149

age. It was found that the test differentiated the special group from the general population. The next step was comparison of the test scores with ratings for the same men by their supervisors. The correlations between their rated proficiency on the job and the different tests are given in table 1. The value of a test in any battery depends on its correlation with the practical criterion and on its intercorrelation with other tests. In the first approximation, it appears that tests 2, 4 and 8 will not add to the discriminative value of the battery since they have a higher correlation with I.Q. than with the practical criterion. The final battery gains little by including in it more than items (1) I.Q., (3) mathematical reasoning, and (7) speed in number cancellation.

Viteles (38, p. 260–322) gives a good picture of tests used for the selection of skilled and semi-skilled workers. His discussion of tests for electrical substation operators is particularly instructive because it reviews the details of all stages of the standardization of a test battery, from job description to application of the tests in hiring new operators. Hazel Benjamin (3) has made a useful survey of articles covering aptitudes and testing procedures for personnel placement and hiring. See also Bingham (4) and Burtt (5).

The present emergency has meant that millions of workers have switched jobs, either in industry or in the armed forces, and many new workers, notably women, have been hired for the first time. Tests play a considerably larger role now than in times when the supply of labor exceeded the demand.

IV. Training. There are few tasks in which robot motor performance suffices. Therefore, imparting intelligent understanding of the job is another important element of training. Closely allied is morale, the factors which motivate the worker to better performance. The present emergency has produced an abundance of examples where workers previously adequately trained, in the usual sense, have increased their output by improving the methods of doing the same job. Ideally, then, training should teach the manipulation, provide understanding as to the principles of motion economy and stimulate a desire for greater accomplishment. Psychological factors are of importance even in strictly physiological training. For instance, in reducing the heart rate in fast-running, attention must be given to psychological principles of motivation to induce the subjects to keep on.

In the process of training men for new occupations, the application of experimentally established psychological principles can both speed up and broaden the training program. In the sense of building a common base for other jobs the question of transfer of skill is very real from the practical point of view. Rapid technological progress is reflected in changing design of machines and manufacturing processes, which in turn require transfer of workers from one operation to another. Under war conditions this displacement has been greatly magnified and readjustment in post-war production will involve the retraining of millions of workers.

J. W. Cox investigated experimentally the changes in performance in assembly operations brought about by drill-like practice as against intelligent training. The problem of ascertaining how practice and training on an assembly operation increases efficiency in related performances required three steps:

1. Testing all subjects, experimental and control, on a number of manual operations
2. Practice or training of the experimental subgroups in a similar operation in which control subgroups did not participate
3. Re-testing all subjects on the initial tests.

The "practice" consisted in repeating a given

assembly operation at maximum speed 440 times. Subjects in the "training" group "were instructed in the general principles underlying the best methods of work, and they carried out formal exercises designed to direct attention to points to be observed in manipulating the material" (6, p. 162). The eleven "training lessons" corresponded in length to the "practice" periods and were given for eleven days. A considerable part of each "training" period was spent in talking about such matters as arrangement of the parts on the bench, improvement and control of performance on the basis of visual and tactile data, and the economy of motion. Exercises in the "training" group were repeated only 85 times, as compared with 440 repetitions in the "practice" group. Retest on the initial five tests showed significant evidence of transfer of skill in the "training" group; the "practicing" group showed very little gain over its control.

Skill, developed by the repetitive practice of one manual operation, contributes little to the performance of other jobs. On the other hand, skill developed through intelligent instruction tends to transfer to a fairly wide range of manual operations. This leads to a practical suggestion that teaching industrial skills should take into account not only the neuromuscular factors but also the controlling mental mechanisms.

The effect of non-financial motivation on the rate of learning is illustrated in an experiment conducted by A. J. Marrow. In a newly organized plant one group of sewing machine operators was informed at the end of the first week that their output ranged from 20 to 25 per cent of the minimum level for a skilled worker and that this standard should be reached in about three months. The discrepancy appeared too great and the prescribed standard was not seriously accepted as a workable goal. "Improvements were slow, learning plateaus common, and after fourteen weeks only 66 per cent of the standard had been reached (18, p. 61). The other group had been given the same information, but, in addition, a definite goal had been set for each week. At this time there were some individuals in the plant who actually had reached the standard. "This combination of an immediate goal for the near future and the acceptance of the final goal as a real standard for the group led to a much more rapid improvement" (18, p. 61). The group surpassed the standard before the end of the scheduled time.

The effect of financial incentives was investigated by S. Wyatt (42) who studied the reactions of a group of 10 young women employees. The work involved packing, weighing and wrapping. For the first nine weeks all workers were paid a fixed weekly wage irrespective of output. The amount of improvement during this time was 12 per cent in terms of the first week's output and continuation of this method of payment did not promise further increase. During the following 15 weeks a competitive bonus system was used in which the slowest worker was given the same wage as before, the next better received an additional sixpence, and so on throughout the group. This produced a sharp rise of 46 per cent in output. When the work-curve practically leveled off, a piece-rate system was introduced. Under this third system output increased an additional 30 per cent and remained on that level.

V. Accidents. During the last 25 years much attention has been directed to industrial accidents. The importance of minimizing the hazards by better machine design and protective devices was well recognized and accident rates were reduced by these measures. Posters, accident museums, repeated newspaper and radio campaigns, and shop-to-shop safety competition were used effectively in further reducing the number of casualties. The latter fact constitutes proof that a percentage of accidents is due to the failure, not of the machine, but of its operator.

The psychotechnologist versed in the techniques of advertising research can compare the effectiveness of the various methods used in safety campaigns in changing the attitudes of the worker and imparting information. However, any mass approach is not fully satisfactory. Accident etiology is complex and includes insufficient information about hazards; temporary indisposition resulting from fatigue, ill health and emotional tensions; acquired habits such as faulty work methods; and permanent personal dispositions (e.g., defective vision).

Accidents are not distributed in an "accidental" or chance manner; certain persons are more liable to have an accident than others. Numerous studies tend to confirm this hypothesis. Viteles presents the results of a study of 321 truck drivers which shows that "14 per cent of the driving force was responsible for 47 per cent of all accidents, 25 men having incurred 211 accidents [out of a total of 533] in three years' time" (39, p. 490). Slocombe also observed unequal distribution of accidents in a group of 625 factory employees who suffered a total of 2,641 injuries. These accidents were, for the most part, of minor character. However, it was also found that "the people with a lot of little accidents were the ones who were having the serious accidents" (35, p. 50).

Accident proneness refers to personal factors and attempts have been made to identify them by means of psychological tests. Farmer, summarizing the results of studies on industrial workers, air pilots and drivers, indicates "that people who are slow and inaccurate on certain sensorimotor tests tend to have a higher accident rate

than others", although "the predictive value of these tests is not high" (10, p. 125). They discriminate well only on the extreme ends of the distribution. Nervous instability is also assumed to be related to accident rate and Farmer expects that progress in the diagnosis of accident proneness will be derived mainly from a direct study of the affective make-up. He is willing to accept the suggestion of Lahy and Korngold (16) that the se otor tests diagnose the accident prone- r as they reflect the effects of emotional An indirect way of estimating emotional ility is by means of the psychogalvanic . Experiments using this technique tend to firm the hypothesis that the more emotional erson is prone to have a higher accident rate.

Farmer makes a distinction between accident proneness which is characteristic of the individual, and accident liability which is primarily environmental and represents the amount of strain placed on a person. Such factors as ventilation, lighting, glare, speed of production and density of traffic, methods and hours of work belong in this category.

Vernon summarized experiences from the first World War which are relevant on this point. Data obtained for workers in a British fuse factory show that "during the 12-hour day period the women experienced nearly three times more accidents than in the subsequent 10-hour day" (37, p. 12). Also, the number of accidents incurred during the last hour of the morning work period on the 12-hour day schedule was five times greater than during the first hour. On the 10-hour day hedule this ratio was only 3 to 1. These facts gested that increase in the accident rate was ue to fatigue of the workers. The fatigue hypothesis of accident causation is, however, not quite convincing: in the night shifts there was a reversal of accident frequency. "The accidents were at a maximum at the beginning of the night and dwindled down fairly regularly till the early morning" (37, p. 13).

These statistical studies of accident causation establish the presence and weight of various factors involved. Another approach is the clinical type of investigation which focuses on the individual, considers all available information and leads to treatment which aims at the rehabilitation of the accident-prone employee. Viteles made an excellent summary of the earlier work with emphasis on the transportation industry (38, p. 276-386).

VI. Boredom and fatigue. Fatigue of an isolated muscle is indicated by reduction in its work output under continued stimulation. Extension of this clear concept to the intact organism leads to much confusion. In modern industry it is not often that work output is primarily limited by true fatigue of the muscles, though this may occur in military operations. In some cases the restriction of accomplishment is purely psychological in origin and in the great majority of cases psychological and physiological factors are combined so as to make clear differentiation difficult. However, it is possible to distinguish between the "feeling of fatigue" and "boredom". Boredom is characterized by discontent, restlessness and yawning, whereas the "feeling of fatigue" appears as weariness and can be relieved only by rest. Fatigue which accompanies heavy or very intensive work is regarded as a subjective sign of physiological changes produced by the work. In some cases, such as sprinting, it is possible to identify and measure some of the physiological changes such as the rise in blood lactate, oxygen debt, and so on. In more prolonged muscular work of moderate intensity physiological signs are not very marked and in studying boredom, which results from light but repetitive work, biochemical analyses are of little help.

In a series of systematic research undertaken by the British Industrial Health (Fatigue) Research Board it was found that boredom was experienced most intensely around the middle of the work period and was associated with a lower and more variable rate of working (43).

Data on the distribution of boredom symptoms among 355 women engaged in repetitive work indicated that "3 per cent showed practically no symptoms, 33 per cent were slightly affected, 38 per cent experienced a moderate degree, 23 per cent suffered severely, and 3 per cent were seldom free of boredom" (44, p. 72). Individuals working under the same conditions show varying susceptibility to boredom. In an investigation of a group of workers employed in filling boxes of three sizes —14 lb., 4 lb. and 1 lb.—ten workers out of nineteen preferred to work with the large size and thought work with small boxes too fussy and troublesome. Six packers found small boxes preferable: the work was more varied and they had a greater feeling of accomplishment. The stated preferences were reflected in output: workers preferring *big* boxes did 5 per cent better with this size but were 6 per cent below the group average in filling small boxes; contrariwise, workers liking small boxes excelled the average by 7.3 per cent and fell 5.1 per cent below on large boxes. The authors pointed out that "these differences are instructive because the movements involved in filling the different boxes were almost identical, so that from the standpoint of capacity, those who were superior or inferior in one process would be expected to be equally superior or inferior in the other" (44, p. 12).

What are the personal characteristics of the boredom-prone individual? Wyatt and Langdon (44) investigated four personality traits: general

intelligence, divided attention ("ability to think of other things while working"), perseveration (interference of the preceeding activity with the following activity), and introversion-extroversion. The differences between the average scores of "least bored" and "most bored" workers were found to be statistically significant for the first and last traits studied. Higher intelligence and extroversion tend to be associated with greater susceptibility to boredom.

Individuals who were classified as "most bored" registered also a higher number of complaints against working conditions. In three plants where studies were made on sub-groups comprising 54, 34, and 26 workers, bored workers registered, on the average, 19 per cent, 23.7 per cent, and 21.3 per cent more complaints.

Workers spontaneously develop antidotes to boredom such as talking, singing and daydreaming. Features introduced and tested experimentally in previous investigations included such factors as rest pauses and changes in the form of work. Wyatt and Langdon studied the effect of recorded music assuming that since boredom is due to an awareness of the monotonous conditions of work, its alleviation will depend upon the extent to which the workers' attention can be distracted from these conditions. The experimental group consisted of 12 women workers engaged in light, repetitive work. Output records under the usual conditions were used as a control. Then, music was introduced at various intervals in the work day. It was found that when there was music from 10:00 to 11:15 the average hourly output for the morning work increased 6 per cent over the preceding period. The difference was statistically significant and as a result the management inserted an hour of music in the middle of each work period for all workers.

A good example of interdisciplinary research on the functional changes in the human organism which result from prolonged work is the study on the fatigue of truck drivers, conducted by the Division of Industrial Hygiene, National Institute of Health (15). The Interstate Commerce Commission, which requested the investigation, wanted an answer to the question: After how many hours of work does the driving of the average qualified driver become unsafe? Because a direct answer cannot be experimentally obtained, the research was focused on the onset and progress of the decline in functional efficiency after various spans of driving. Three groups of drivers were tested: I, men who were fresh and had not driven since a major sleep; II, those who had driven less than 10 hours; and III, men who had driven for more than 10 hours. Each man was given a general medical examination and as many as possible of the 22 special tests. These were classified into performance tests which determine the ability to accomplish a task and non-performance tests which measure bodily states over which the subject has little or no voluntary control.

Muscio (23) has emphatically recommended the non-performance tests. However, these experimenters held a different opinion: "Since our knowledge of fatigue is still elementary, it was decided to use every promising avenue of research available in the hope that a characteristic psychophysiological complex might be revealed" (15, p. 20). This more catholic approach proved rewarding: the performance tests showed, on the whole, a more marked and a more consistent fatigue trend. Speed of tapping, simple reaction time, reaction-coordination time, manual steadiness and body sway showed the closest relation with hours of driving: ". . . the men who had not driven since sleep performed with the greatest average efficiency, the men who had driven 0.1 to 9.9 hours were less efficient, and the men who had driven 10 hours or more were least efficient of all" (15, p. XVII). Flicker fusion frequency which stands on the borderline of psychological and physiological functions also showed a consistent decrease. As far as the non-performance tests are concerned, no great and consistent changes were found. The average leucocyte count was lower for the working than for the rested drivers but did not differentiate between the men who had more and those who had less than 10 hours of driving. In a similar way the driving resulted in a slightly lower heart rate and slightly higher mean systolic and diastolic blood pressures. "No appreciable correlation was found between hours of driving and differential leucocyte count, altered knee jerks, dermographia, the specific gravity of the urine, the urine pH, or the hemoglobin content of the blood" (15, p. 55).

A summary of physiological data on fatigue, with special reference to industry, was made by Dill *et al.* (7) and Sayers (32).

VII. Morale. High output is frequently considered a practical criterion of the morale of workers. In this sense placement, training, accident prevention, etc., have their bearing on morale.

The Hawthorne studies (29, 40) drew attention to a number of other important facts: industrial production has to be understood as social behavior; informal organization within the shop and pressures exerted by it significantly influence the output; and problems of internal equilibrium within the industrial organization are as important as the problems of economic efficiency and are amenable to scientific investigation.

Their first test group worked at three consecutive levels of illumination (24, 46, 70 foot candles), while the control group was submitted to illumination of a constant intensity. Production increased

to approximately the same level both in the test and in the control group. It took the "tough-minded" experimenters a few years to realize that other variables were entering into the experimental situation besides illumination: the workers felt that they were participating in a significant project, that they were important as people and not merely cogs. This factor of motivation was more effective than physical changes in the environment. Of course, one cannot draw a general conclusion that environmental factors are of no [illegible]. Too many data from well controlled [illegible] where the effects of learning and [illegible] were taken into account point to their [illegible]ce. Whitehead specified that "in order to [illegible]ain a satisfactory material situation . . . the [illegible] physical situation at any time must be within [illegible] indifferent range of the individual experiencing [illegible]t" (40, I, p. 94).

The illumination experiments at Hawthorne were followed by a five-year study on the effect of various work conditions, either experimentally induced (length of the work day, length of the work week, number and duration of rest pauses, supply of refreshments) or inherent in the situation (hours of night rest, menstruation, temperature and humidity, daily and weekly work cycle). The experimental group consisted of five girls who worked in a separate room and were treated more as collaborators than as "factory hands". A number of changes in work conditions were made, e.g. two rest pauses were introduced and working hours were reduced. The output increased. This was considered remarkable "as [illegible] of the operators had assembled relays for a [illegible]derable time previously and had reached [illegible]me sort of steady state in their working skill" (40, I, p. 240). However, when the original work conditions (full 48 hours week, no rest pauses) were restored, the expected drop in output did not occur and a high level of efficiency was maintained. This was a shocking experience and it pointed more emphatically to the importance of work attitudes as production factors.

Daily and weekly variation in output could be traced in part to physical and physiological variables. Output decreased slightly for two or three days of the menstrual period. The same was true of exceptional spells of cold or hot weather. On the other hand, slow seasonal, weekly and daily changes of temperature and relative humidity had no detectable effects on the output rate. A significantly greater part of the variation in output was found to be related to inter-personal stimulation, and production records showed frequently a high degree of co-variation for pairs of operators. The relation between the work-rates of pairs of workers was not a stable quantity but varied more or less synchronously with the socio-emotional relationships of the individuals.

The Hawthorne experiments in the Bank Wiring Observation Room further revealed the character of output as a "form of social behavior," and industrial organization as a complex social system. The experimental group included nine wiremen, three soldermen and two inspectors. Records of quantity and quality of output were kept as in previous studies. Two methodologically important features were added: systematic interviews and full-time observation. The observer, stationed in the room, had the function of a record keeper and of an objective, disinterested spectator without executive authority. The interviewer remained outside the group. His task was to elicit and record the worker's feelings about the job, his co-workers and supervisors; his personal history; his social contacts outside the plant. Restriction of output despite the incentive payment plan was one of the significant discoveries of this experiment. The group attempted to work at a more or less identical pace and various devices were used to achieve this end. Social pressure was exerted against the "slaves" who tended to maintain a higher output rate.

In 1936 a new interviewing program was begun at Hawthorne which became known as the personnel counseling plan. It was considered as the specific function of personnel work in industry and was differentiated from general functions, such as employment routines, training, accident prevention, wages and collective bargaining. The role of the counselor was defined as "that of carefully listening and observing, of making diagnoses, and then stimulating the most effective action on the part of the various other agencies in the structure [of the industrial organization] whose formal function is to deal with the particular problem under consideration" (29, p. 601).

The counseling plan at Hawthorne suggests that mass maneuvers aimed to increase morale (appeals to loyalty to the plant and to the feeling of patriotism, increase in wages and job security) has to be supplemented by an individualized approach. Handling of employees' adjustment problems on the professional level was demonstrated by Viteles (39, p. 369–392 and p. 586–611) in dealing with rehabilitation of accident-prone taxi drivers and vocational maladjustment. Highly trained personnel cooperated in an interdisciplinary diagnosis and treatment of the worker problems. The approach was an adaptation of the clinical method of individual study developed at the University of Pennsylvania by Witmer for dealing with behavior problems of children. A series of interviews enabled the consulting psychologist to understand the dynamic structure of each case and to work out a readjustment program with a

committee including the company physician, social worker, garage superintendent, street supervisor, and assistant general manager.

SUMMARY. A brief review has been made of ways in which psychological factors are involved in motor performance. In addition to some theoretical problems in the field of psychosomatics, attention has been paid to criteria of efficiency, industrial job requirements, training, accidents, boredom and fatigue, and morale.

It has been stressed throughout that problems of industrial performance are complex and that adequate research demands an interdisciplinary approach.

Among the scientific disciplines which enter into the study of human work, physiology and psychology occupy positions of first importance. It is hoped that this review may help to indicate some directions in which cooperative research would be fruitful.

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PERFORMANCE IN RELATION TO ENVIRONMENTAL TEMPERATURE

REACTIONS OF NORMAL YOUNG MEN TO SIMULATED DESERT ENVIRONMENT

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When first exposed to hot environments most men are incapable of working strenuously or for prolonged periods. Such work is performed inefficiently and leads to disability in many men. By a process of acclimatization man adapts himself to work in the heat. He then works as efficiently as in temperate environments, without subjective complaints and with little or no disturbance of bodily functions. A consideration of performance in relation to high environmental temperatures must, therefore, immediately concern itself with the problems of acclimatization to heat for it is largely in this aspect that performance in heat differs from performance in temperate environments. Most other factors governing performance exert similar influences at high and low environmental temperatures. Because of its paramount importance in performance in the heat this study will concern itself largely with the problem of acclimatization to heat and more specifically to dry (desert) heat.

Acclimatization to heat appears to be a complex physiologic readjustment which cannot be defined adequately or determined completely by a few imple physiologic measurements. Nevertheless, adaptation is accompanied by certain physio- hanges which can be measured and which as general indices of the entire process. It is in this sense of an index of the problem rather than a complete understanding that the following observations are presented.

MATERIALS AND METHODS. A preliminary period of two months was spent in the desert training area of California during August and September, 1942 in order to obtain information on the nature and scope of the problem, particularly from the point of view of the Army. In the present study the observations were carried out in simulated desert conditions produced in the "hot room" of the Laboratory. The duration of the exposure in the hot room varied from one to three weeks. Prior to exposure to the heat, the men were given a period of training in order to harden them. Their physical fitness was estimated before and after preliminary training, immediately on exposure to the heat and after acclimatization to the hot environment. These estimates were based on their performance for moderate work of long duration (marching) and severe work of short duration ("pack" and "step" tests).

The temperature of the room was maintained at 120°F from 8:00 A.M. to 5:00 P.M. and at 90°F from 6:00 P.M. to 6:30 A.M. One hour was required to change from one temperature to the other. Relative humidity was kept as low as possible and ranged from 15% to 22% during the day. During the day wall temperatures were in equilibrium with the air temperature while the floor was 8°F to 10°F cooler than the air. No additional radiant heat was supplied. The environment was, therefore, less rigorous than that of the desert with the same air temperature and humidity. A moderate degree of air movement was obtained from two 26-inch fans or four 10-inch fans but the rate was not measured. Since the studies were carried out during the five months beginning with October the experimental environment represented an extreme change from that to which the subjects were previously exposed.

Experimental subjects. The experimental subjects were 56 enlisted men; 48 lived continuously in the hot room except for two five-minute periods for lavatory privileges taken when the temperature of the room was 90°F. The age limits of the men were 17 and 43. Only three were over 30 and the majority were between the ages of 20 and 28. None of the men had had recent infections and all were healthy. They were in different states of training and manifested varying degrees of physical fitness.

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Clothing. Some observations were made with men wearing different types of clothes in order to study their effect on heat balance of the body. For most of the experiments in the hot environment, however, the men wore what they chose, usually cotton shorts, socks and regulation shoes. Fatigue clothes were worn during the period of preliminary training.

Preliminary training. Because the physical condition of the experimental subjects was not constant, the men were trained for at least one week in a cool environment (70°F to 76°F) before being subjected to the hot environment. During this period the work was similar to that which they were to perform later in the heat.

Test groups. Group I, the walking group. It was the largest of the four. These men performed work of moderate severity and duration, namely, walking at the standard army pace carrying a 20-pound pack. A walk of two and one half miles in 47 to 50 minutes constituted a "work period." Between successive work periods a rest period of 10 to 13 minutes was given during which observations were made. Unless disabled, the men walked two successive work periods in the morning and three in the afternoon, walking a total of 12.5 miles a day. The data and conclusions of this report are based, for the most part, on observations made on men performing this type of work.

Group II, bicycling group. Men in this group performed a fixed amount of work pedalling a bicycle ergometer for 10 minutes in each of two successive hours in the morning and three successive hours in the afternoon. Observations were made before, during and after work.

Group III, resting group. Men in this group were allowed to rest during the first three or four days in the hot room before beginning work and during this period did no more than was required for subsistence.

Group IV, intermittent exposure group. Eight men lived in their barracks and were subjected to the hot environment for four hours in the morning, returning to their quarters after each exposure. While in the hot room they walked for two work periods separated by an hour of rest. These men all had their initial exposure on the same day. They were then divided into pairs for re-exposure. At intervals of three days a new pair was re-exposed to the heat. Once a man had received his second exposure to heat, he returned to the hot room every third day.

Food. Regular army fare was provided the experimental subjects from their own mess and consisted of the rations allotted to the soldiers doing regular duty. No record was kept on the type or amount of food eaten.

Water and salt. Salt was added to all drinking water to give a final concentration of 0.1 per cent salt solution. The water intake was measured and was administered according to one of three schedules: (a) As much as desired whenever wanted, (b) Adjusted to equal the total weight loss, (c) Restricted to 4 liters daily, approximately one half the amount lost, and given in one of two ways: (1) 270 ml every hour from 6:00 A.M. to 6:00 P.M. plus 750 ml from 6:00 P.M. to 6:00 A.M. (2) 750 ml at 6:00 A.M., 1250 ml during the noon hour, 1250 ml with the evening meal and 750 ml from 6:00 P.M. to 6:00 A.M.

Sleep. Eight to nine hours a night were allowed for sleep. A few men had difficulty in sleeping on the first night of the experiment but most slept well throughout.

General observations. Each morning and evening the rectal temperature, pulse and respiratory rates were recorded. Each morning the weight was measured to $\pm\frac{1}{4}$ lb., and the twenty-four hour urine excretion was measured and samples taken for chloride determination. Special emphasis was given to the general appearance and subjective reaction of all men during the work periods and records were kept of the vigor, "morale", sweating, flushing of the face and any complaint of headache, gastroenteric or cardiovascular disturbances. Rectal temperature was recorded at the beginning and at the end of each work period. The heart rate was measured at the beginning and at the end of each work period with the subject in both the erect and supine position (3 minutes in each) and at 15-minute intervals during the working period (subject marking time). Auscultation over the precordium was necessary to count accurately the more rapid rates. The blood pressure was determined at the beginning and end of each work period in both supine and erect positions (3 minutes in each). Posture was changed either voluntarily or by use of a tilt table. The weight, within 5 grams, was recorded at the beginning and end of all work periods. All clothes were removed and the sweat dried off. The water intake and urine output during each work period was carefully recorded.

GENERAL RESULTS. The factors involved in performance in the heat and in acclimiatization to heat are presented by a series of representative charts. Although these charts indicate the observations on a single man, or a small group of men, it is to be understood that they are typical examples and are supported by other similar observations.

Comparison of acclimatized and unacclimatized states. The unacclimatized man works in the heat with a high pulse rate, a high body temperature and an unstable blood pressure, particularly after change in posture (chart 1). Compare, for example, the performance on the fifth and first days in the heat.

With continued exposure and work in the heat, acclimatization ensues and the heart rate, rectal

temperature and blood pressure return to levels approximating those obtained after similar work in cool environments. This is true with the subject erect or supine (chart 1).

Of particular interest are the changes induced by the assumption of the erect position after

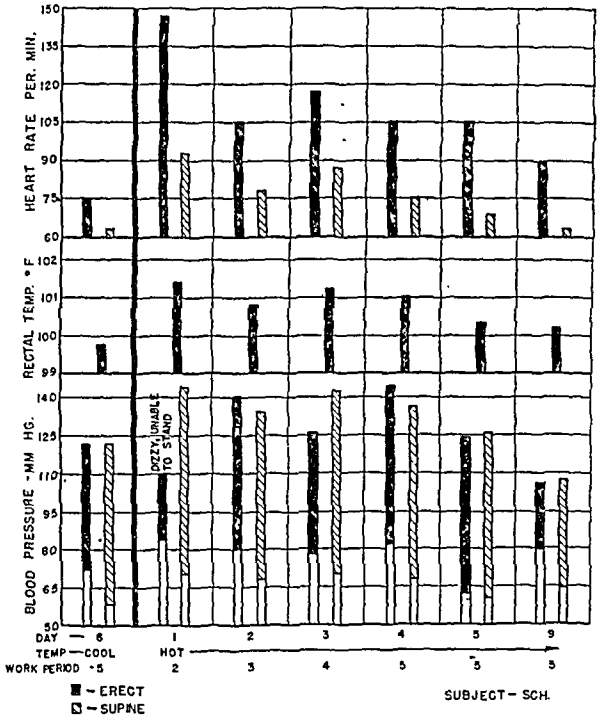

Chart 1. Progressive improvement in heart rate, rectal temperature and blood pressure in the erect posture as acclimatization develops.

The charts (except no. 13A) are similarly plotted. Along the ordinates heart rate, rectal temperature and blood pressure are charted in turn. The total height of the column indicating blood pressure represents the systolic pressure; the white portion of this column (limited by the transverse line) indicates the diastolic pressure; e solid or hatched portion of the column gives ulse pressure. Along the abscissae are in- ed the day of work, the environment in which work was performed and the period of work at the end of which the plotted data were obtained. A key with each chart interprets the hatching of the columns. The text associated with each chart indicates whether the data were obtained from single observations or averages.

cessation of work. In the unacclimatized state (first day in heat, chart 1) change of posture causes marked alterations in cardiovascular dynamics, as indicated by pulse rate and blood pressure. In the erect posture the heart rate is markedly accentuated, the systolic blood pressure falls and the pulse pressure narrows. As a result of the lowered blood pressure the cerebral circulation at times becomes inadequate, symptoms of cerebral hypoxia arise and syncope may ensue. Lying down promptly slows the heart rate, restores the blood pressure and dispels the symptoms of cerebral ischemia.

Table 1 indicates the incidence of syncopal attacks in men standing quietly erect after working in the hot environment. In all instances syncopal symptoms or signs, usually both, appeared within 3 to 5 minutes of the completion of work and were sufficiently severe to force the men to lie flat. When syncope appeared imminent, the men were tilted flat before unconsciousness occurred.

It is apparent that this type of circulatory inadequacy disappeared as work in the heat was continued and in many subjects this clearing was rapid. Some men stood without difficulty following a second work period on the first day, after having a syncopal episode following the first work period. Once postural circulatory inadequacy disappeared

TABLE 1

Incidence of syncopal attacks in the erect posture after working in the hot environment

DAY OF WORK IN HEAT	NUMBER OF MEN WORKING	NUMBER OF MEN HAVING SYNCOPE	PER CENT INCIDENCE OF SYNCOPE
First	45	20	44.4
Second	38	8	21.1
Third	37	3	8.1
Fourth	37	1	2.7
Fifth or later	38	0	0

usually it did not recur on subsequent days of work in the heat. The decrease in number of fainting attacks paralleled the development of acclimatization.

Although observations were made with the subjects both erect and supine, in this report performance is evaluated for the subjects chiefly in the erect posture and all charts (unless otherwise indicated) refer to such measurements. Three facts led to this decision; (a) the findings in the erect posture paralleled those in the supine, (b) the erect posture places an added strain on the physiologic functions of man, revealing disturbances not apparent when man is supine, (c) a useful man is a working man; work usually requires the upright posture.

Although a low heart rate, a low rectal temperature and a stable blood pressure generally accompany acclimatization, one cannot define the process or detect differences in the degree of acclimatization between individuals by such simple measurements alone. This is illustrated by the data for four subjects plotted in chart 2. On the

fourth day of exposure to heat all four men successfully completed five work periods at which time subject Bel. had the most rapid heart rate and the highest rectal temperature. This might be taken as an indication of incomplete acclimatization and evidence that Bel. was not as capable of work in the heat as the other three men. His general appearance and behavior, however, indicated that he was more fit than Ham. or Gee., both of whom had lower heart rates and body temperatures. On the following (5th) day, the men worked under more severe conditions. Subject Ham.

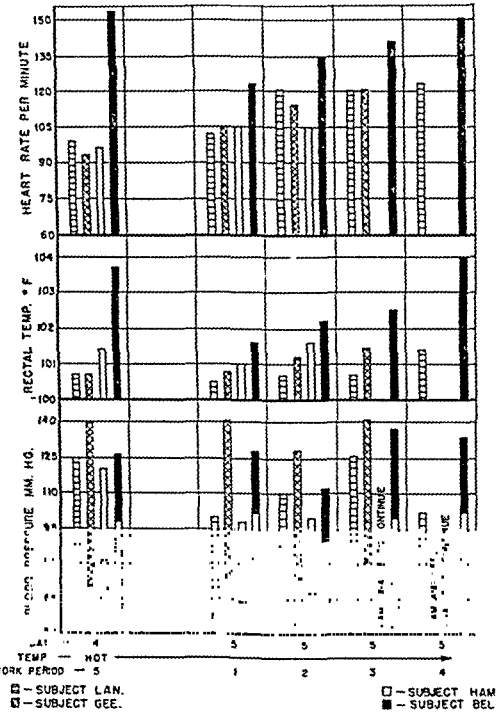

Chart 2. Failure of heart rate, rectal temperature and blood pressure as sole criteria of performance in desert heat.

became weak, nauseated and vomited after the second work period and could not continue. Subject Gee. was forced to stop at the end of the third work period because of exhaustion. Subject Bel. with a heart rate and rectal temperature which were always higher than those of Ham. or Gee., continued energetically for another work period and on finishing appeared almost as fit as Lan. Thus, prediction of performance on the basis of heart rate and rectal temperature alone did not agree with the actual performance of these men.

Undoubtedly a man, doing a fixed amount of work, is less efficient and more prone to disability when his rectal temperature and pulse rate are high, than when they are low. However, individual performance is influenced by many variables which are not evaluated by such simple measurements. It is necessary to consider and evaluate each man as a whole and to avoid focussing attention on the rectal temperature or heart rate. The man's subjective symptoms, his objective appearance, his behavior and his actual performance must receive at least equally careful consideration in any evaluation of his capacity to work in the heat.

The acclimatized man is alert, performs his work energetically and without symptoms. Usually his heart rate and rectal temperature are low, at least not markedly elevated. On the other hand the unacclimatized man working in the heat becomes dull and apathetic, performs his work poorly, has a rapid heart rate and a high rectal temperature and may manifest to varying degrees, and either singly or in combinations, the symptoms and signs of heat exhaustion. In the present experiments we came to recognize the unacclimatized men by the following symptoms and signs: *Symptoms* (1) fatigue (2) headache (3) dizziness, especially when erect (4) shortness of breath (5) loss of appetite (6) nausea (7) vomiting (8) abdominal cramps; *Signs* (1) flushing of face and neck (2) rapid pulse rate (140–200/min) (3) lack of coordinated effort (clumsy, stumbling) (4) staring glazed eyes (5) mental disturbances (apathy, poor judgment, irritability) (6) fever over 102°F (7) collapse.

Of special interest is the marked flushing of the face, neck and upper chest which occurs in almost all men when they first work in the heat and which disappears as acclimatization develops. It is first noted approximately one half to one hour after undertaking work in the heat for the first time and develops into a pronounced and at times slightly cyanotic erythema. It begins around the cheeks and eyes and extends to occupy the entire face and ears, frequently being detected in the skin of the chest as well as the neck and upper extremeties. The flush is associated with subjective and objective warmth. The skin is hot to the hand and its temperature, as determined by a radiometer is significantly increased. Frequently there is an engorgement of the conjunctival and scleral vessels so that the eye appears bloodshot and it may even be mildly painful.

Some men when first exposed to the heat have had a period of "sniffles", associated with an engorgement of the mucous membrane of the nose, though this has not been constant. After a work period during the early days of exposure to heat, swelling of the hands is often noticed. The men carry packs, and although constriction by the shoulder straps may contribute to the edema, it nevertheless occurs in men who walk without packs. Even though the men continue

to carry their packs, it tends to diminish or disappear as acclimatization progresses.

FACTORS IN ATTAINING AND MAINTAINING ACCLIMATIZATION IN A HOT ENVIRONMENT. As pointed out above, when different persons are compared, the heart rate, rectal temperature and blood pressure are not, in themselves, completely reliable measures of ability to maintain an excellent level of performance in the heat. Nevertheless, they may be utilized as indices of acclimatization when they are consistent with the other above-discussed evidences of acclimatization. It was with these limitations in mind that the heart rate, rectal temperature and blood pressures were used as indices in this study. The factors involved in attaining and maintaining acclimatization to heat are presented in a series of charts and it is to be understood that the plotted changes in rectal temperatures, pulse rate and blood pressure were consistent with the picture of the man as a whole. When they were not, specific mention of the differences are made.

Course of acclimatization. The process of acclimatization appears to be initiated by the first exposure to heat. This is indicated by chart 1, in which are plotted typical observations made on one man at the close of the last work period of each charted day. Considerable improvement in heart rate, rectal temperature and blood pressure (in the erect posture) is apparent on the second day in the heat, that is, after one day of exposure.

At the close of the last (second) work period on the first day in the heat this man was very tired, giddy and unable to stand erect. On the second day he finished three work periods feeling much better than on the previous day, had no difficulty in standing and maintained a normal blood pressure in the erect posture. Thereafter he worked without difficulty.

In most men a major portion of the improvement in ability to work in the heat is attained by the ... or fifth day of work in a continuously hot ...onment. This is illustrated in chart 3 which ... the progressive changes recorded in two groups of men exposed to heat at different times. Each column represents the average of the data obtained on four men at the end of the last work period of the day indicated. During the first three to four days there is a progressive and rapid improvement in heart rate and rectal temperature, which thereafter levels off at values somewhat higher than those obtained under similar circumstances in the cool environment.

Physical condition. Although exceptions occur, men in good physical condition generally acclimatize to heat more rapidly than men in poor condition. Moreover, the fit men are capable of a greater work-output in the heat with less symptoms and less disturbance of their heart rates, rectal temperatures and blood pressures than are the less fit men. In this study the determination of physical fitness was based on the work performance of the men while in a cool environment. In evaluating physical fitness all of the factors previously discussed (the appearance and behavior of the man as well as the results of physiologic measurements) were taken into consideration. Those men were considered most fit who performed the prescribed work easily and energetically, without symptoms and with least disturbance of their heart rate, blood pressure and rectal temperature.

The three men whose records are compared in chart 4 were from a group of eight men whose

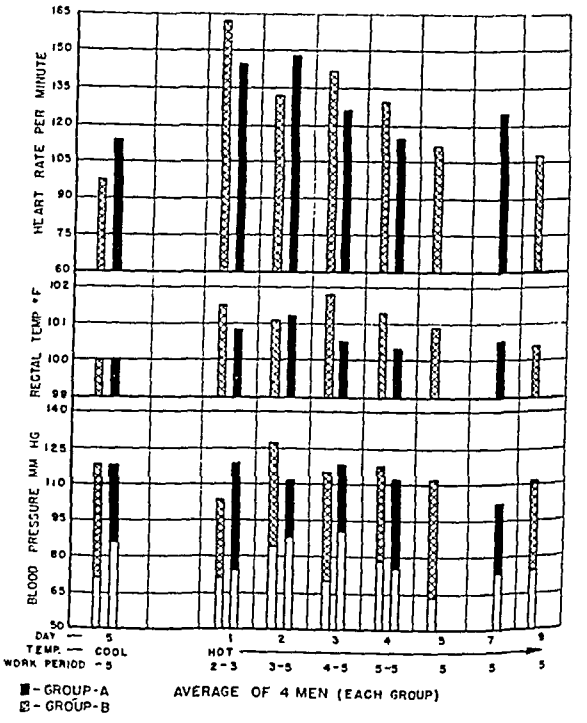

Chart 3. The course of the development of acclimatization as indicated by the heart rates, rectal temperatures and blood pressures in two groups of men exposed to desert heat at different times.

physical fitness was assessed before they entered the hot environment. Three different observers gave independent ratings. All three observers placed subject Sch. first. Two observers placed subject Kit. seventh, one observer sixth. Two observers placed subject Lup. fifth, one observer second. Of the three men, Sch. was considered most fit, Kit. least fit, and Lup. intermediate between the two.

Observations on each of these three men were obtained at the end of the last work period on each of six days in the hot environment and compared with measurements made on the last day in the

cool environment (chart 4). The more rapid improvement in the pulse rate and rectal temperature of subject Sch. is readily apparent. An equally rapid improvement took place in the general appearance and behavior of this subject. By the second day he was walking easily and with vigor. Note also the maintenance of blood pressure when erect. In contrast to Sch., the pulse rates, rectal temperatures and blood pressures of subjects Kit. and Lup. returned more slowly toward control levels. The general appearance and behavior of these two men likewise indicated a slower rate of acclimatization and subject Kit. always seemed to work with difficulty. Even after acclimatization had been attained by all three men the performance of Sch. was superior to that of the other two men (see 9th day in hot environment). On the fifth hot day subject Kit. was prevented from walking by blisters on the feet.

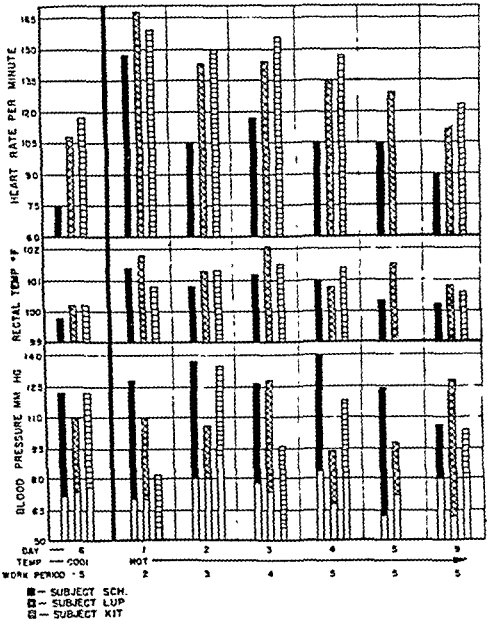

Chart 4. The effect of physical condition on the rate of development of acclimatization and on the efficiency of work after acclimatization has been attained.

Activity prior to and during acclimatization. Continuing the preliminary training period in a cool environment beyond that required to develop a satisfactory state of physical fitness does not increase the subject's tolerance to heat on first exposure. Resting in the heat for the first three days increases considerably the ability to work in heat but the acclimatization thereby induced is only partial. Acclimatization is developed most rapidly by the daily performance of work in heat from the outset, the amount of work being progressively increased within the capacity of the individual.

The relative effect of these three factors on the process of acclimatization was determined, using twelve subjects divided into three equal groups. After the same preliminary training for all men, one group (group A) continued to work in the temperate environment. The other two groups were taken into the hot environment and of the two, Group B rested while the other (group C) immediately undertook graded work which was progressively increased. When group C was acclimatized (4th day) all three groups were subjected to the regular work schedule in the hot environment.

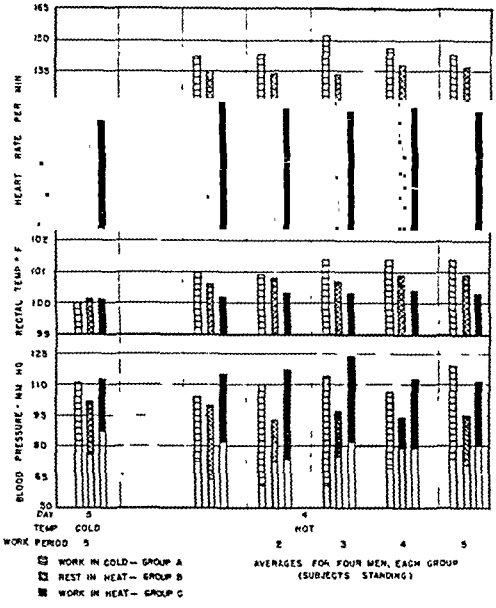

Chart 5. The comparative effects of prolonged training in the cold, of rest in the heat and of graded work in the heat on the performance of men in desert heat. The observations were made with the subjects in the erect posture.

The comparative behavior of the three groups is striking (charts 5 and 6). The performance of the subjects in group C (graded work in heat during the previous 3 days) was substantially similar to their performance in the cool environment, with only slight elevation of heart rate and rectal temperature over the control levels. In contrast, the subjects in group A (working in heat for the first time following extended preliminary training) gave no evidence of acclimatization. The heart rate and body temperature was high in all men.

Only two of the four men completed the prescribed work and the condition of these two was considerably worse than that of the other men in the other groups. The performance of the four men in group B (resting in heat during the previous 3 days) fell between the other two groups. All four men completed the required five work periods. Although the heart rates and body temperatures were higher than in their control state, and also higher than in group C, the performance of these men was consistently better than that of the men in group A. Thus, a partial state of acclimatization had been induced by rest in heat alone.

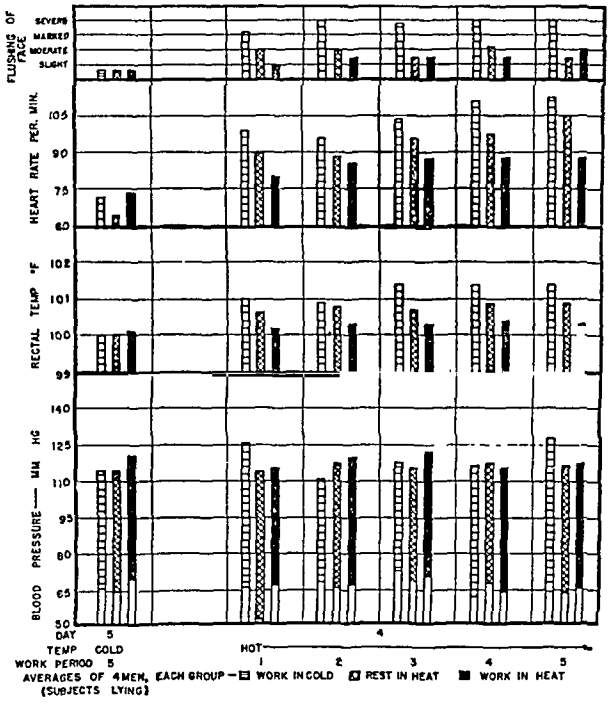

Chart 6. Same as chart 5 except that the data is for the subjects in the supine position.
The severity of the facial flush parallels the other evidences of lack of acclimatization to heat.

Continued strenuous work from first exposure to heat. Strenuous work on first exposure to heat is not well tolerated. Twelve (12) unacclimatized men were asked to perform the full five work periods (12.5 miles) on their first day in the hot environment. Four men became exhausted (after the third or fourth period) and were unable to complete the task. The eight who completed the work did so with difficulty, finishing in poor shape and with high heart rates and rectal temperatures. The ability to complete strenuous work in the heat on the first exposure does not necessarily indicate acclimatization nor the ability to continue to work in the heat. Maintaining work at a strenuous rate from the outset leads to a progressive deterioriation of performance. After two or three days many men become disabled and those who continue to work do so ineffectively and inefficiently. This is in contrast to the progressive improvement of men subjected to a schedule of gradually increasing work in heat.

The performance of one of the subjects illustrates this point (chart 7). The data were obtained at the end of each work period on the last day in the cool environment and on each day in the heat. During the first day in the heat this subject completed five work periods with only moderate difficulty. On the second day in the heat, however, he could complete but three work periods. On the

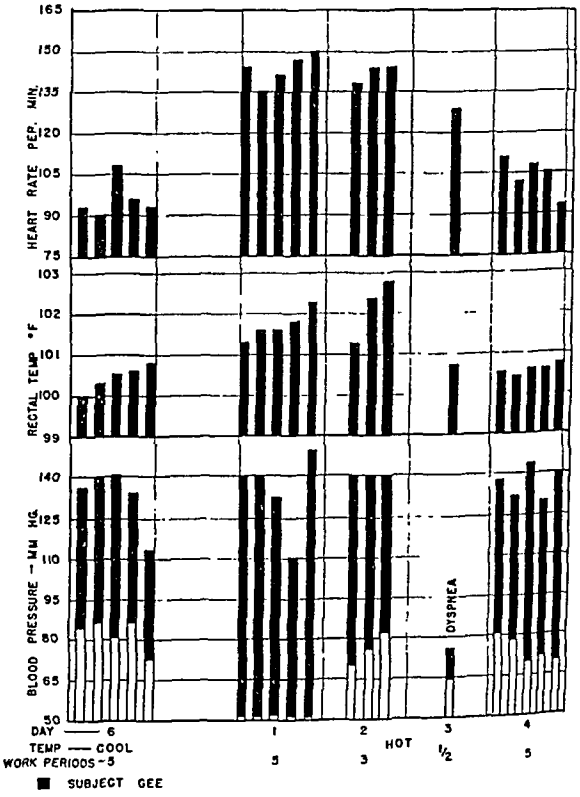

Chart 7. The effect of maintaining strenuous work from first exposure to heat. Progressive deterioration of performance and disability results.

third day he was forced to stop in the middle of the first period. It is of interest to note the low blood pressure on this day in contrast to the more nearly normal rectal temperature and heart rate and to compare these data with those obtained at the end of the fifth period of the first day in the heat, at which time he was still in fair shape. After dropping out in the first period of the third day, this man rested the remainder of that day and drank much salted water. On the next (4th) day he finished five work periods in good condition and with a heart rate and rectal temperature approximating those recorded after similar work in the cool environment. Despite the exhaustion result-

ing from too strenuous work during the first three days in the heat, this man had attained a large degree of acclimatization by the fourth day.

Intolerance to heat and heat exhaustion. Development of symptoms of intolerance to heat and even heat exhaustion during the early days of exposure to heat do not retard the rate or decrease the degree of acclimatization finally attained, *provided* that when such disability occurs work is discontinued, rest is permitted and water and salt are given. When work is resumed it should be within the capacity of the individual.

Chart 7, which illustrates this, has already been discussed. Chart 8 represents a similar, but more severe, situation in another subject. The data

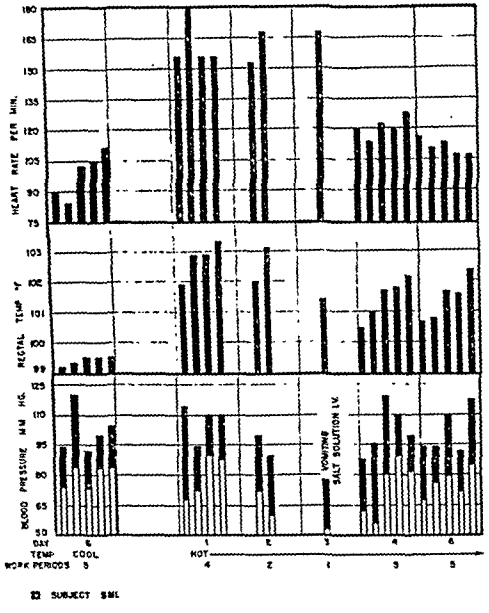

Chart 8. Heat intolerance to the point of heat exhaustion does not retard the development of acclimatization if rest, water, and salt are provided when disability occurs.

obtained at the end of each work period of each day in the heat are plotted and compared with the observations on the last day in the cool environment. On the first day in the heat this man could complete but four work periods when fatigue forced him to discontinue. On the second day he finished only two work periods; on the third day only one. Note the high heart rates and rectal temperatures reached on these days and the progressively decreasing blood pressure (chart 8). The appearance and behavior of the subject likewise indicated a progressing deterioration. On the third day he was quite ill; exhaustion, abdominal cramps, nausea, vomiting and marked apathy indicated heat exhaustion. After a liter of physiologic salt solution was administered intravenously the nausea, vomiting and abdominal cramps ceased. He rested for the remainder of that day and drank salted (0.1 per cent) water copiously. On the next (4th) day and the days thereafter he completed five work periods without difficulty, always finishing strongly and appearing to be acclimatized. This improvement was accompanied by a reduction of the heart rate to values equalling those obtained in the cool environment but the rectal temperature continued to rise to high levels (102°F.).

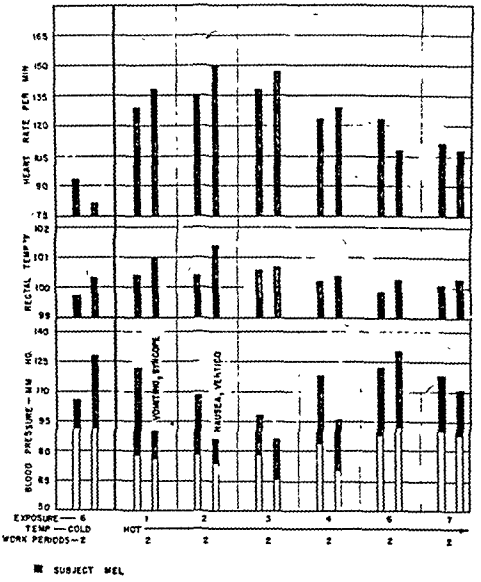

Chart 9. Course of the acclimatization resulting from intermittent (every third day) short (4 hours) exposure to desert heat.
Compare with charts 1 and 3; continued exposure to heat.

Single exposures to heat at intervals of three days. The following three conclusions are based on data derived from eight subjects who performed two periods of work during a four hour exposure to heat every third day and who spent the intervening time in a cool environment: (1) A single relatively short period of work in the heat induces but little acclimatization, (2) a number of such exposures separated by two days in the cool environment results in acclimatization, (3) the major portion of this acclimatization, for the above work requirement, is produced by three or four such exposures to heat.

Representative observations on subject Mel., taken at the end of each work period during the four-hour exposures to heat, are shown in cha-

During each exposure two periods of work were performed, separated by one hour of rest. The first exposure to heat was badly tolerated and caused weakness, nausea, vomiting and syncope when in the erect posture. The second exposure produced similar but less severe symptoms and vomiting was absent. Thereafter work in the heat was accomplished without difficulty and with increasing ease. The associated changes induced in the heart rate, rectal temperature and blood pressure, and their regression, paralleled the findings already described for subjects continuously exposed to the hot environment. (Compare chart 9 with charts 1 and 3.) In this subject there was a particularly striking postural hypotension during the first three exposures to heat with a return of

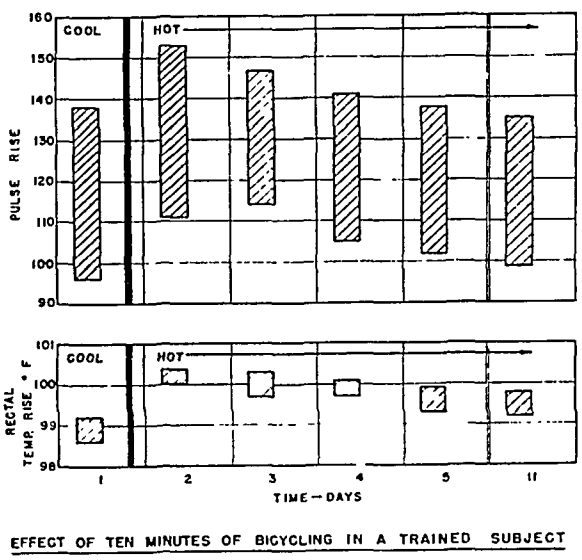

Chart 10. Course of the development of acclimatization to severe exertion of short duration (bicycling 10 minutes each hour).
Compare with charts 1, 3 and 9.

the blood pressure to normal as acclimatization developed.

Short periods of severe exertion. Men performing severe work of short duration in the heat show changes, which in their pattern and readjustment are similar to those following less severe work of long duration (marching). The severe exertion consisted of pedalling a stationary bicycle for ten minutes each hour. The observations plotted in chart 10 are from a typical subject and were taken at the end of the first "ride" of each day.

The high rectal temperatures and pulse rates produced by this exertion become progressively less marked as work in the heat is continued. Levelling off is attained by the fourth or fifth day. In one respect the readjustment differs from that observed for the more moderate work of marching. The resting level, rather than the increase caused by work, determines the final level of the pulse rate and body temperature. Most subjects found these short bouts of severe exertion less fatiguing than the prolonged but moderate work of marching.

Rest at night. Adequate rest at night is essential for good work performance in the heat, even in acclimatized men. Deprived of it, men work inefficiently the next day.

The data obtained on subject Mel. after the last (second) work period of each day are given in chart 11. This subject belonged to that group which performed two periods of work during a four hour exposure to heat every third day. The night before

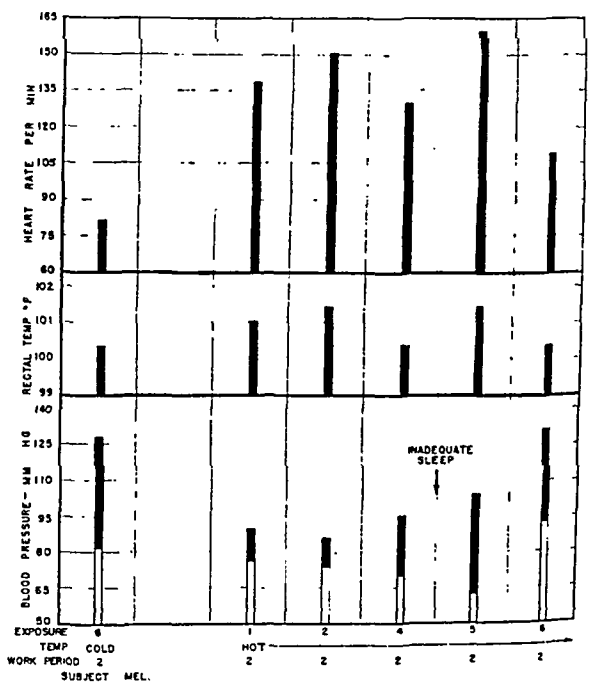

Chart 11. Temporary deterioration of performance resulting from inadequate rest on the previous night.

his fifth exposure he failed to obtain adequate rest. His performance during the next day was almost as poor as that on his first exposure to heat and he completed the work with difficulty. Here again the true state of the subject is not indicated by the heart rate and rectal temperature. During the fifth exposure they are higher than during the first and second, yet the subject was in a better condition. There was no headache, nausea, vomiting or syncope in the erect posture, symptoms which had rendered him totally incapable of further effort on the first day in the heat.

The poor performance during the fifth exposure to heat did not retard further improvement. Note the much improved performance during the sixth exposure.

Duration of acclimatization to heat. After removal from the hot environment acclimatization to desert heat is well retained for at least one week and probably for two weeks. Thereafter, a variable but more rapid loss ensues so that after one month the major portion of the acclimatization is lost by most men. Some men, however, retain a considerable degree of acclimatization for two months after leaving the hot environment.

The data plotted in chart 12 were obtained on seven men at the close of the last work period on the following days: The last day in the cool environment (diagonal-lined column), the first day in the hot enviroment (cross hatched column),

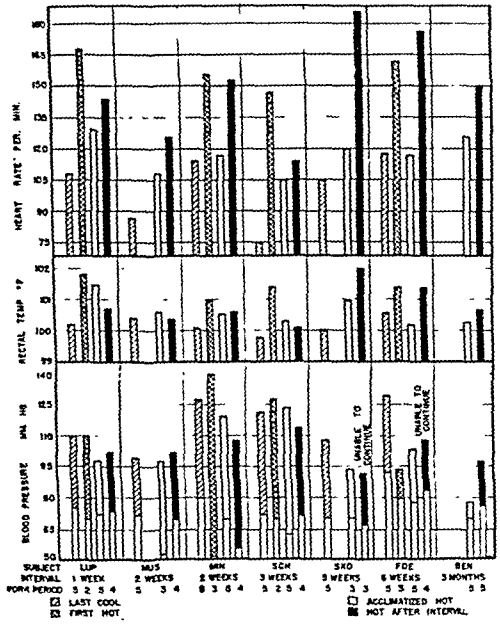

Chart 12. Duration of acclimatization to heat after removal from the hot environment.

when fully acclimatized (open-block column) and the first day of re-exposure to heat (solid column). The observations for each individual are grouped together and separated by long vertical lines. "Interval" indicates the time between leaving the hot environment and first re-exposure to it.

After two to three weeks there was a sharp loss in acclimatization as indicated by the failure to complete as many work periods, by the poor appearance of the subjects and by the high heart rates and rectal temperatures (Sko., Foe., Ben.). The vigorous and alert appearance of subjects Lup., Min., and Mus., and the ease with which they completed their prescribed work indicated a high degree of acclimatization despite their higher heart rates and rectal temperatures. Subject Sch. worked as well in the heat after a lapse of three weeks as when fully acclimatized.

Maintenance of acclimatization to heat. There are two requisites for the maintenance of a high degree of performance in the heat over a long period of time: *a.*, the maintenance of good physical fitness and *b.*, repeated exposures to heat, preferably with work, at intervals of one month or less.

Of the three subjects considered in chart 12A, subject S was never in good physical condition, subject M remained moderately fit and subject W only fairly so. The strikingly poor performance of subject S when he walked in the heat after a lapse of 37 days indicated that he had not only

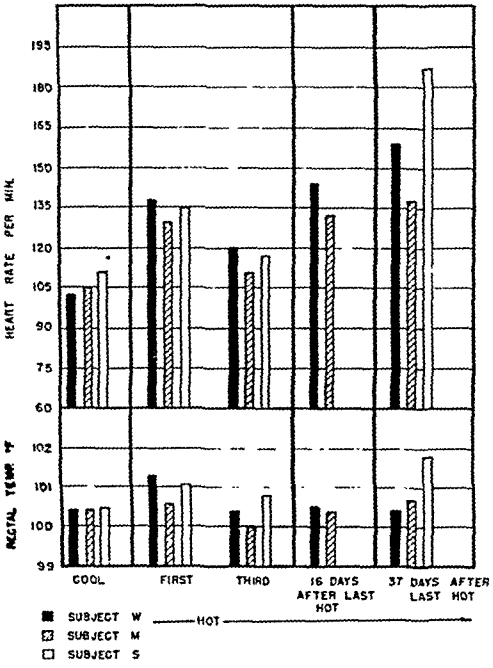

Chart 12A. The relationship of physical fitness to the retention of acclimatization after removal from the hot environment.

lost all of his acclimatization but was in far worse condition than at any previous time. This was attributed to loss of fitness as well as of acclimatization in the interval.

The more fit subject (M) had a much better work performance than the less fit subject (W) when re-exposed to heat after a lapse of 16 days and 37 days. This was indicated not only by the lower heart rate and rectal temperature of subject M but also by the fact that of the three men re-exposed to heat after a lapse of 37 days he was the only one able to complete the five work periods.

The need for re-exposure to heat in order to maintain acclimatization is indicated in chart 13.

Here are plotted the observations made on one subject at the close of each work period on the last (5th) day in the cool environment, on the first four days in the hot environment, and on re-exposure to heat 44 and again 47 days after leaving the hot environment. Initial acclimatization to heat was rapid and by the third day, five work periods were performed without difficulty and with heart rate, rectal temperature and blood pressure approximating those for the cool environment. On the first re-exposure to heat 44 days after leaving the hot environment, the subject was unable to continue after the fourth work period. At that time he was almost exhausted, the heart rate was

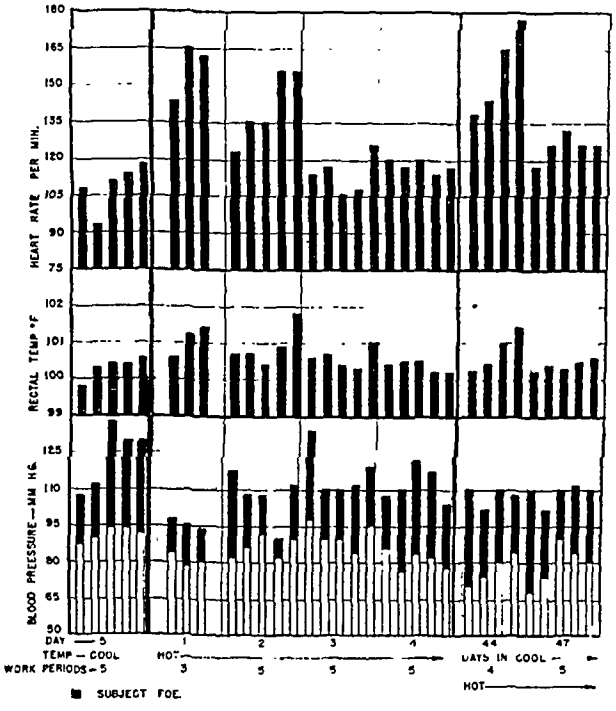

Chart 13. Reacclimatization following a single work exposure in the heat after loss of previous acclimatization due to prolonged absence from the hot environment.

more rapid than at any other time and the rectal temperature was high. But this exposure re-induced a great deal of acclimatization for on a second re-exposure to heat three days later he was able to work as long and almost as efficiently as he had when well acclimatized to heat 47 days previously.

Water requirements. In desert heat man maintains a normal body temperature only by virtue of the cooling effect produced by the evaporation of the water of sweat at the skin surface. If proper tissue hydration is to be maintained and bodily functions continue efficiently this lost water must be replaced. The amount of water lost, and hence the water requirement, is best indicated by the loss in body weight either over a unit of time or during the performance of a given task (here a walk of 2.5 miles).

Chart 13A is a histogram of the weight lost by the men in the hot room during rest and during marching. The data indicates that men carrying a 20 pound pack and walking 2.5 miles per hour lose about one liter of water per hour. This loss and requirement is the same whether the men are acclimatized or unacclimatized, whether water is restricted to one-half of the required amount or forced to amounts equal to the weight lost. The requirement for acclimatized men at rest was one-half of that at work; one-half liter.

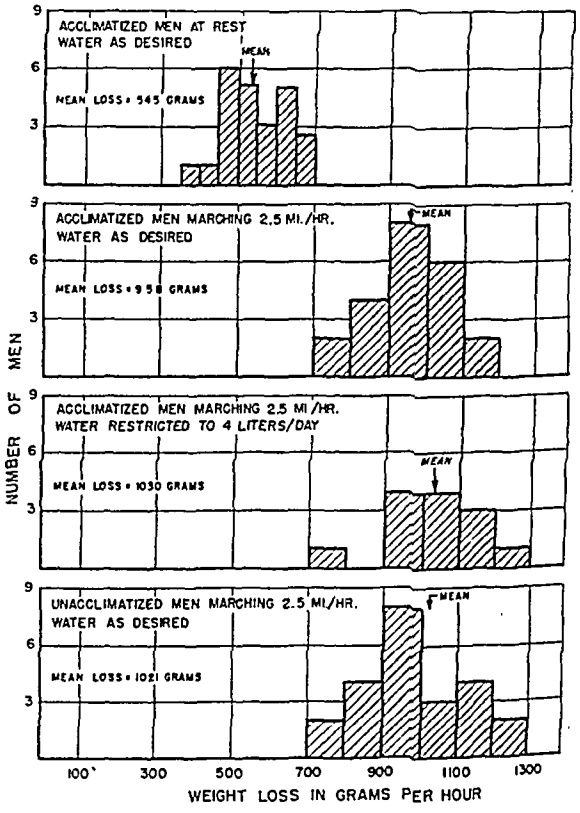

Chart 13A. Rate of weight (sweat) loss of resting and working men.

Increased water intake. Thirst is an inadequate guide to the fluid required to work in the heat. No man drank enough water voluntarily to replace that lost in the sweat while working and all developed water deficits. Increasing the water intake during work to an amount (1200 ml. per hour) equal to the water lost by sweating increased the amount of work which was accomplished on the first exposure to heat.

Twelve men were asked to work the full five periods during their first day in the hot room. Nine men received water in amounts sufficient to quench their thirst (600 ml. per hour), 3 received water in amounts (1200 ml. per hour) equal to the

weight (sweat) lost. These three men all finished the five work periods without great difficulty. In contrast, four of the other nine men became exhausted after three or four work periods and could not continue. Those who did finish were in poorer condition than the men whose water intake was intentionally increased.

In chart 14 the effects of slight water restruction (6 liters per day) are compared with those of full water replacement (9 liters per day), in two groups of three men each, on their first and fourth days in the hot environment. Each column represents the averaged data for the group. Observations

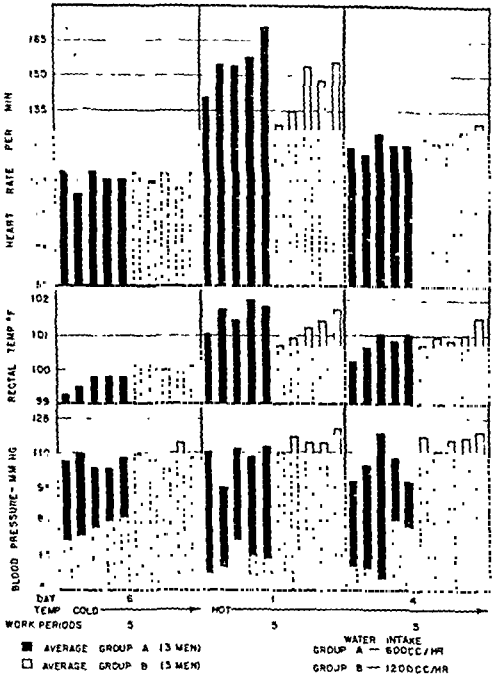

Chart 14. The comparative effects of slight water restriction and of full water replacement on performance during initial exposure to heat and on the development of acclimatization.

were made at the close of each of the five work periods on the last day in the cool environment and the first and fourth days in the hot environment. In order to determine whether the course of acclimatization had been altered by the changed water intake all men in both groups were permitted to drink as much water as they chose on the fourth day. Men who did not complete five full periods have been excluded.

Although the group in which water was forced to full replacement showed smaller disturbances of vigor, behavior, pulse rate and rectal temperature during their first day in the heat, the degree of acclimatization attained by both groups by the fourth day was the same.

Water restriction. Sudden restriction of the water intake of well-acclimatized men at work to one-half of the optimal requirement induces changes similar to those which appeared in the men on first exposure to heat when they were unacclimatized.

In chart 15 are plotted observations made on each of four well-acclimatized men. Their performance at the close of each work period on the day (9th) when water was restricted to 4 liters per day is compared with that following the fifth work period on a day (4th) when they received as much water as they desired. The deterioration in performance resulting from water restriction is apparent in the higher pulse rates and rectal

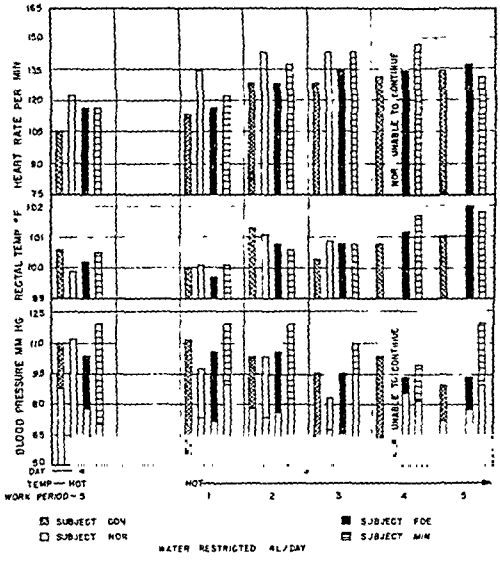

Chart 15. The effect of water restriction on the performance of well acclimatized men.

temperatures and the low blood pressures. Subject Nor. was incapable of continuing after the third period and the other men finished five periods with difficulty.

An important change which the chart does not show was the actual condition of the men, their low morale and lack of vigor, their glassy eyes, their apathetic, torpid appearance, their "don't-give-a-damn-for-anything" attitude, their uncoordinated stumbling, shuffling gait. Some were incapable of sustained purposeful action and were not fit for work. All they wanted to do was rest and drink.

Progressive restriction of water was tolerated better than sudden restriction. For sudden restriction the intake was reduced on one day to

4 liters. Progressive restriction was carried out by limiting the intake from the optimum level of 8 L/day to 6 L for the first day, 5 L for the second and third day and to 4 L for the fourth day. The gradual restriction of water intake resulted in physiologic disturbances similar to, but less severe than, those observed from sudden water restriction. Again men were incapable of performing as much work as when water intake was adequate.

Cross acclimatization to jungle heat. Acclimatization to dry (desert) heat increases markedly the ability of men to work efficiently and effectively in moist (jungle) heat.

Three men were fully acclimatized to desert heat and six men were trained to work in a cool environment. All nine men then worked in a simulated jungle environment; dry bulb 90°F to 91°F, wet bulb 88°F to 89°F, relative humidity 90 per cent to 96 per cent. The averages of the data obtained on each group of men at the close of the last work period in the cool environment, and at the end of each work period of the first day in the hot moist (jungle) environment are compared in chart 16. The performance in desert heat, (as expressed by average data for the desert group) is plotted between the heavy vertical lines. The first column represents observations made at the close of the fifth work period of the first day in the desert heat; the second column, the data from the fifth work period of the third day, when desert-acclimatized.

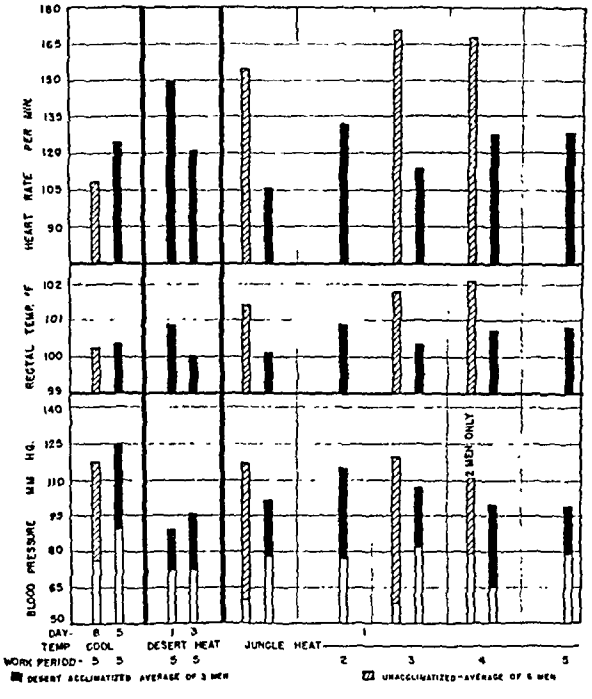

Chart 16. The effect of previous acclimatization to dry (desert) heat on the ability to work in moist (jungle) heat.

On the first day in hot moist (jungle) heat five work periods were completed by each of the desert-acclimatized men; two men finishing strongly and easily and the third with some difficulty. Of the six men not previously exposed to a hot environment, four were able to complete only two periods of work, the first and third, while the other two completed three, the first, third and fourth. Not only were the desert-acclimatized men capable of a greater work output but the work was performed more efficiently than was the smaller amount of work done by the other men.

The performance of the desert-acclimatized men, however, was not quite as good as it had been in the cool and desert environments.

Discussion. A consideration of performance in hot environments immediately resolves itself into the problems of the unacclimatized man and the problems of the acclimatized man.

Of the factors influencing performance in the heat the process of acclimatization is of greatest importance. The present study does not pretend to explain the mechanism of this complex process nor does it present all the known physiological changes associated with this amazing adaptation. Our rather empiric observations do, however, clarify the general principles governing acclimatization to heat and indicate the need for regulating the activity of men according to these principles if they are to work effectively and efficiently in the heat without undesirable symptoms and without disability.

Except for a relatively small number of "heat tolerant" individuals most men experience undesirable and even disabling symptoms on attempting hard work when first exposed to the heat. These effects are of varying severity in different subjects but as a rule they cause most men to perform as "unfit" men who must be trained, i.e., acclimatized, for their environment. The physically fit may be affected as severely as the unfit. Until acclimatization is attained a man in excellent physical condition may, on working in the heat, be reduced to an extremely poor physical state or even become completely disabled. In the unacclimatized state, therefore, the concepts of performance and physical fitness based on observations in temperate environments are not always valid. Because of this, it is not possible on the basis of tests performed in temperate environments, to predict which men will suffer greatest disability when first working in the heat. As acclimatization ensues the more fit subject again becomes capable of a greater and more efficient performance than the less fit. In the acclimatized state, the concepts and criteria of fitness and performance formulated in temperate environments again hold true. Since acclimatization is usually readily (4–5 days) attained it follows that

the physically fit man is the best man for work in the heat, just as in any other environment. It is merely necessary to train him properly through those several days when he is rendered temporarily unfit by the hot environment.

The performance of the acclimatized man in the heat is influenced by the same factors as those which influence his performance in a temperate environment. However, since the hot environment imposes a basic load in addition to the work, performance in the heat is more readily disturbed by those factors which impair performance in any environment; loss of rest, lack of food and lack of water and salt. Of these the lack of water and of salt are especially critical. Only by the evaporative cooling of his sweat can man live and work in desert heat and only by replacing the water lost in the sweat can work and life be continued. When the water loss is not replaced performance deteriorates greatly and rapidly (within hours) and if the water deficit is maintained disability results. Since much salt is lost with the sweat it too must be replaced, otherwise the depletion of bodily stores of chloride leads to a deterioration in performance.

Aside from the above discussed consideration peculiar to and imposed by the hot environment, performance in the heat, like performance in the cool, is dependent on physical fitness. A discussion of the nature of physical fitness, methods of determining it and its relation to performance fall beyond the scope of this communication which deals rather with the effect of hot environment on performance. Nevertheless a consideration and evaluation of physical fitness formed an integral part of our observations.

Like acclimatization, physical fitness appears to be a complex physiologic manifestation not completely defined in all of its aspects, difficult to measure quantitatively among members of a group. Again like acclimatization, physical fitness cannot be defined nor can differences be detected by means of a few simple physiologic measurements (heart rate, body temperature, blood pressure) obtained during limited tests (step test, pack test, long march). To do so results in focussing attention on some small segment of the whole process and this at times gives an entirely erroneous concept. Man is not a pulse rate, a rectal temperature, but a complex array of many phenomena. The same is true for acclimatization, physical fitness and performance. It is always necessary, therefore, to consider the man as a whole—his behavior, appearance, complaints, physiologic measurements and from this whole draw an estimate of these complex processes.

Into performance enters the baffling yet extremely important factor of motivation, the will-to-do. This cannot be measured and remains an uncontrollable, quickly fluctuating, disturbing variable which may at any time completely alter the performance regardless of physical or physiologic state.

How greatly character is affected by a hot environment has scarcely been approached in any study. Nonetheless, in the heat, as in the comfort zone, character, as well as physique and physiological state, determine performance.

SUMMARY

1. Performance in hot environments depends greatly on the state of acclimatization.

2. A man acclimatized to heat works in the heat with a lower body temperature, lower heart rate and a more stable blood pressure, than when not acclimatized. Nevertheless, acclimatization to heat cannot be measured by these criteria alone, as they do not necessarily correlate with the man's behavior and ability to work. The man as a whole must be considered and evaluated.

3. Acclimatization to heat begins with the first exposure, progresses rapidly and is well developed by the third or fourth day.

4. Subjects in good physical condition acclimatize more quickly and are capable of a greater work output in the heat than are men in poor physical condition.

5. Continued training in cool environments beyond that necessary to attain good physical fitness does not further increase the ability to work in the heat nor shorten the period of acclimatization.

6. Resting for three or four days in the heat, with activity limited to that required for subsistence, results in definite, but only partial acclimatization. Some work in the heat is necessary for complete acclimatization.

7. Full acclimatization (the ability to perform a maximum amount of strenuous work in the heat) is attained most quickly by graded, progressively increasing work in the heat.

8. Strenuous work on first exposure to the heat is not well tolerated and will often result in disability. If such work is maintained for several days many men will become incapacitated and those who continue to work do so ineffectively and inefficiently.

9. Intolerance to heat on first exposure, even to the point of heat exhaustion, does not retard the rate of acclimatization or lessen the degree which is finally attained, *provided* work is discontinued when symptoms appear, water and salt are given, and subsequent work is within the capacity of the subject.

10. Three or four exposures to heat of 3 or 4 hours duration with two one-hour work periods during each exposure, will produce a considerable

degree of acclimatization. These exposures may be separated by intervals of two days in a cool environment.

11. The pattern of acclimatization is the same for short severe exertion as for moderate work of long duration.

12. Inadequate rest at night results in less work or less efficient work on the ensuing day, even by the well acclimatized man.

13. Acclimatization is well retained for one to two weeks, after which it is lost at a variable rate. Most men lose the major portion of their acclimatization in one month—a few are able to retain it for two months. Men who remain in good physical condition retain their acclimatization best. Repeated exposures to heat are required at intervals not exceeding one month, if a high degree of acclimatization is to be maintained for long periods of time.

14. The amount of work accomplished on first exposure to heat can be increased by drinking water in amounts equal to the weight (sweat) lost during work. The rate and final degree of acclimatization attained are not influenced by the water intake (forced, moderately restricted, or taken as desired) during the first two or three days of work in the heat, *provided* that after this initial period men are permitted as much water as desired.

15. Suddenly restricting the water intake of men working in the heat leads to a deterioration of morale and motivation, reduces greatly the efficiency with which work is performed, decreases the total work output and causes disabling symptoms in many men. This holds for even the well-acclimatized man. Gradual reduction of water intake induces changes similar to sudden restriction, differing only in that they are produced more slowly.

16. Acclimatization to hot dry (desert) environments increases markedly the ability of men to work efficiently and effectively in hot moist (jungle) environments.

REFERENCES

We are acutely aware much work has been done, and is in progress in the field we have discussed. We have omitted a bibliography because the lack of library facilities at an army post has precluded anything but the most cursory survey of random selections.

PHYSIOLOGICAL FITNESS FOR THE DESERT

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How does the desert tax the human body? Heat often comes to the body at rapid rates from sun and air. Water is sacrificed by the body to dissipate that heat; sources from which to replace the water are few. The circulation is driven faster to transport heat to the body surface for dissipation. Salt is expended in sweat. The alimentary tract is called upon to absorb unusual quantities of water and salt; and to resist any diarrhea or vomiting that will rapidly deplete the body of these substances. The same wind that helps to evaporate the sweat also brings dust to lungs and eyes. The same incessant sun that heats the body exposes the eyes to glare and the skin to burn. Such are the unusual stresses that make demands upon the physiological equipment of man. They differ only quantitatively from those in more habited climes.

Physiological fitness is a proper study because men are functionally unequal. By fitness I refer to those properties that make or break a man's performance. There are, therefore, just as many kinds of fitness as there are kinds of performance expected of him. It seems preferable to consider those broad types of performance that fall to every man who has no air-conditioned space to work in. What difference does it make in those performances whether he is in the desert or in a more popular community?

Heretofore fitness has been studied with respect to athletic performance and to flying performance. It seems that the activities of living in the desert require as much fitness and deserve detailed study.

Fitness varies. Evidence that fitnesses differ among individuals is found when men are given a fixed rate of work in 8-hour days (fig. 1). Some then are able to complete this work at much higher temperatures than others. At any one humidity, a frequency distribution of individuals appear with respect to maximal temperature. Those who can perform only at the lower temperatures are handicapped compared to their fellow workers.

Humidity has a large effect in determining how high a temperature can be endured; in the low humidities a percent decrease in relative humidity is almost as helpful as a Fahrenheit degree dimi-

nution in temperature. At rest the effect of humidity is less. Clothing helps a man to endure dry heat and sunshine; but in wet heat may be a hindrance. A temperature of 130°F with a relative humidity of 10 per cent is maximal for most desert areas.

Every group of people in the desert recognizes that some individuals can endure extreme conditions longer than others. Some work at a fast pace, others at a slow pace, quite aside from their differences in another climate. Some are exuberant when others are dispirited. What functional bases can be found for these differences? If such bases are once understood, fitness can be assessed.

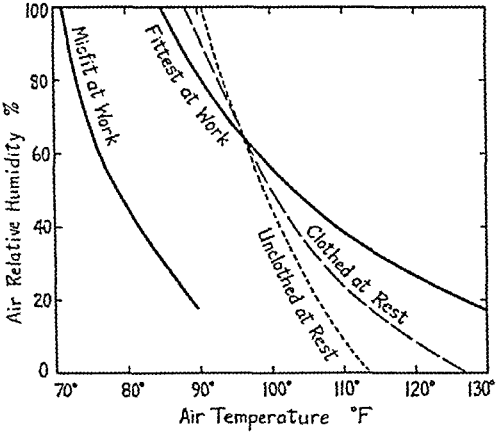

Fig. 1. Climograph for upper limits of temperature and humidity endured by men indoors. Solid lines enclose the *range* of conditions that can be tolerated by diverse men working at a moderate standard pace, according to data of Newburgh, Herrington and Gagge (1943). Broken lines indicate *average* of conditions just endured by certain men at rest with and without clothing; data from Winslow, Herrington and Gagge (1938, p. 701).

How do men come to possess these differences? Are men created unequal? How much is born in them, how much is developed in early life, and how much is latent, to be manifested after repeated exposures?

With respect to heat dissipation, it is clear that a man without sweat glands is unfit. With respect to reception of radiation, an albino individual is under grave disadvantages. Hence, some of the grosser forms of unfitness are congenital.

Probably many factors have only a partially congenital basis. Kuno (1938a) found that the number of *active* sweat glands is significantly greater in Filipinos than in Russians. But this was not necessarily an inherited characteristic, for the number of active glands becomes greater during the first two years after birth (Kuno, 1938b). The suggestion is that exposures to heat in those years may permanently augment the the available glands. Possibly this phenomenon represents an opportunity for any race to develop a population of super-sweaters who can later revel in the desert.

The size of each sweat gland increases throughout childhood (Kuno, 1938b), allowing considerable latitude in its functional performance, it may be supposed. So some factors of fitness are inherited, some are developed (perhaps partially in accordance with use), and some are acquired by acclimatization.

Acclimatization. The difficulties presented to the human body by hot atmospheres are easiest seen in their extremes. In early work in hot rooms I found (Adolph, 1924) that men became exhausted to a state of *circulatory* failure. This shock-like collapse represented an inability of the peripheral blood flow to fulfill the demands made upon it. It meant that the transport of heat to the body surface taxed the circulation continuously and immoderately. At that time it was not suspected that the circulation of blood has any means of obviating its difficulties.

Many years later, this time in the desert itself, I saw the processes of acclimatization going on (Adolph, 1938). I saw myself doing tasks on the tenth day after arrival in June in Boulder City, Nevada, that were utterly impossible on the first day. Acclimatization was a real thing; it involved circulatory adjustments to promote losses of heat whereby the body temperature stayed low even in rapid work (fig. 2). Heat was now dissipated by more ready production of sweat. It was also apparent that individuals differed enormously both before and after acclimatization (Dill, 1938, p. 42).

The sweat glands functioned more readily after acclimatization. During standard walks, instead of freely secreting sweat only after the rectal temperature became elevated 2 or 3 Centigrade degrees, the body now formed enough sweat before the temperature had risen one degree. Dill *et al.* (1938) showed also that the concentration of salts in the sweat diminished when the body temperature stayed lower; this resulted in a marked conservation of salt in the body, as though faster sweating involved less escape of solute.

Yet acclimatized individuals differed among themselves in respect to circulatory performance, sweat formation and salt conservation. Those individuals who sweated easily were not always the same ones who secreted the most dilute sweat. In fact there was no apparent correlation; and this illustrates the fact that separate sieves are required to detect the various virtues which men may possess.

The changes in response of the body to repeated

or continuous exposure often make the difference between success and failure in the desert. The striking aspect is that *all* the known changes are such as tend toward success and comfort. In a sense, a new physiological constitution is temporarily acquired.

The circulatory system behaves differently after exposures to heat by reducing the initial venous engorgement (Scott *et al.*, 1940), by promoting blood flow without pooling in the periphery, and by diminishing the pulse rate. The body temperature is thus kept low during moderate effort (Adolph, 1938). Sweating is now elicited more readily through the usual reflexes

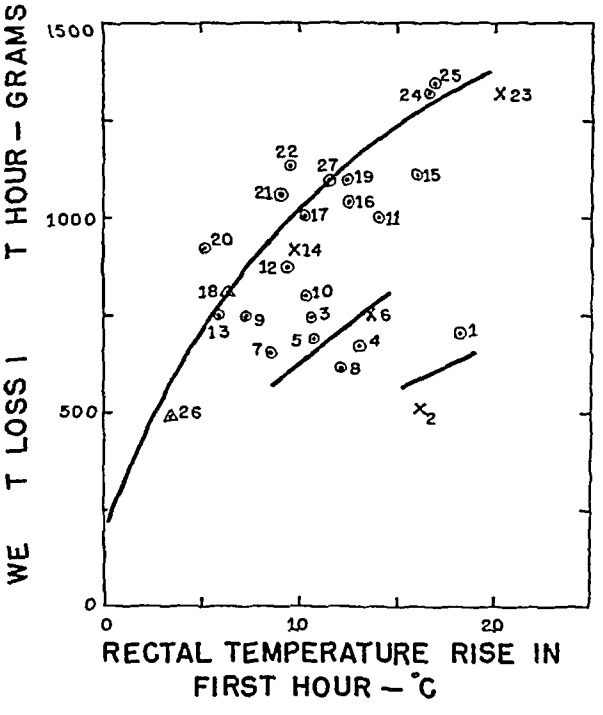

Fig. 2. Losses of weight by sweating in relation to gains of rectal temperature in the first hour of daily walk in one man. The days of exposure to the desert are numbered serially; the air temperature varied on diverse days. From Adolph (1938, p. 494).

and through the humoral and local stimulations of sweat glands. The body has become prepared for actions that combat heat at a lesser provocation. Somewhat more water is used to dissipate the heat, for the body temperature is lower despite somewhat more gain of heat from the environment.

Other circulatory changes upon exposure to warm temperatures have been described. Such are: transient increase in plasma volume and in whole blood volume (Bazett *et al.*, 1940), temporary increase in cardiac output, increase in blood flow in fingers (Scott *et al.*, 1940), and gradual decrease in rate of basal oxygen consumption (Burton *et al.*, 1940). It is noteworthy that most of these modifications are temporary, as though they were first aids to getting along with the heat; these aids later become unnecessary. Even the loss of heat by radiation is said to improve after the first two or three days of exposure (Burton *et al.*, 1940).

One important question is: does acclimatization to heat hold equally for conditions of intense radiation, of high convection ,and of humid tropical atmospheres? Or is it specific for each? No doubt the responses of acclimatization overlap considerably; but in so far as heat is dissipated differently in the several environments, different degrees of modification may exist in the constituent processes. Acclimatization occurs even when no work is done. In fact it is likely that there are just as many kinds of acclimatization as there are kinds of fitness; and fitness is by definition different for each precise environment and each kind of duty.

How it feels to be catapulted into the desert unacclimatized is vividly pictured by Stott (1936). Engine trouble required an airplane to land 13 men in Arabia at 4 a.m. of a summer day. By noon the temperature was 125°F and the men were unable to stand without breathlessness. When a rescue plane arrived at 2 p.m. only 11 of the 13 were able to walk with the greatest difficulty the mile necessary to board the new plane.

What is this acclimatization which does such great things physiologically? It seems to be a latent capacity that comes to realization under appropriate stimulation. One hypotheses is that the range of environments may be so great that the organism cannot at one time be ready to cope with all of them to the optimal extent. Hence it shifts its readiness so as to meet the most prevalent circumstances. The properties which allow this shift are none the less inherent, in so far as they come to realization when elicited.

But the ability to acclimatize varies greatly *among* individuals (Dreosti, 1935). Just as circulatory functions and neuromuscular responses differ, so the modifications that these functions and responses undergo when stimulated also differ.

Acclimatization to the desert is as rapid as it is dramatic. For two or three days in the summer desert a man is uncomfortable and lazy. Upon about the fourth day he suddenly finds life enjoyable again. He wants to be vigorous. In some individuals changes can still be detected after ten days (as, in rates of sweating, Adolph, 1938); and it is very likely that some processes are still approaching asymptotic rates for many weeks or months.

Fortunately, acclimatization to the desert once acquired is retained for several weeks of non-exposure. Intermittent exposure is efficacious in

inducing the characteristic changes; indeed, development of them probably proceeds in intervening periods. A few hours of initial exposure have detectable effects a week or two later, for then the pulse is not so greatly accelerated by a given stress.

The characteristics of men which change with acclimatization to heat are, therefore:

Pulse rate	decreases
Pulse pressure	decreases
Body temperature	decreases
Rate of sweating	increases
Concentration of sweat	decreases
Basal O_2 consumption	decreases
Work output	increases
Endurance	increases

How appraise fitness? Since fitness is a set of characteristics that can be identified, it can be measured. It is measured by performances in extreme conditions. While these conditions are predominantly those of heat, it seems unwise to leave out of consideration any characteristic that is related to performance.

Perhaps the fit of a man to the desert can be likened to the fit of a glove to the hand. The glove is expected to fit mechanically, and also to fit functionally. A person who has but one pair of gloves has to use them on bitter cold days and on merely cool days. So the desert is not fixed in what it requires of the man; on some days he encounters intense radiations, on other days hot winds, on other days dense dust. But the man who fits the most prevalent conditions with most functional adequacy, is the man who finds himself at home in the particular part of the desert in which he is.

What are the human characteristics which are optimal for work in the desert? No one is interested in the fitness of a man who will stay in bed or in an air-conditioned car all the time he is in the desert. Therefore, the duties to be performed enter into the assessment of fitness. Those duties either in war or in peace are so various that no one of them can be picked as typical. For, some new machine may revolutionize desert duties sooner than a physiologist can design new tests of fitness.

For these reasons it seems advisable to recognize only general catagories of fitness. A man may be expected to walk but not to run; to stand but not to stand long at attention; to coordinate but not to do mathematical research. Therefore, physiologists might agree upon some sort of walking test, some sort of postural test, and some sort of manipulative test. Shall the performances emphasize perfection, rate, endurance or all three?

Criteria of fitness in the desert are of at least three sorts. They may (1) characterize the performance of those who have formerly lived in the desert for some length of time; they may (2) represent men who are fully acclimatized; or they may (3) take as fit, men having high values of those measurements that are known to become high during acclimatization. In every case men who do similar activities in some other climate are serving as control. In each comparison those men who endure longest or accomplish most in certain tasks are considered most fit.

(1) So far no description appears to be available for the characteristics of men who formerly lived with success in the desert.

(2) Lendon (1938) attempted to find which traits belong to the fit man by comparing soldiers who had been in Peshawar (India) for 5 years or more with those who had been there for $\frac{1}{2}$ year or less. The former had lower basal rates of oxygen consumption, lower blood urea and sugar concentrations, and lower blood chloride concentration following a march. They sweated more for the same exertion. It is by no means certain that all these functions regularly differ from those in the newcomer. But if they do, were the men who stayed 5 years selected from others who did not stay, or did fitness come upon them in course of time? Probably both factors appeared in mixture, and at present no one is able to tell whether natural selection among individuals, or impact of environment upon the individual, conferred most of the fitness.

Extensive investigation of groups of people living in semi-desert climates has failed to reveal clear biochemical or physical differences from those in temperate climates (Sundstroem, 1926; Talbott *et al.*, 1933; Dill *et al.*, 1940).

The working capacity is much greater in men whose dissipation of heat is readier. Their mechanical efficiency is also slightly greater in a critical range of temperatures (Robinson *et al.*, 1941). In a given individual the efficiency is less in the heat than in cool atmospheres (Yaglou, 1937).

(3) A provisional description of the fit man is provided by the characteristics which change as men acclimatize. Whatever properties (*e. g.*, rate of sweating) numerically increase during acclimatization, those same properties may be expected to be higher in the fitter man. This useful criterion is derived from the universal evidence that the acclimatized man is fitter than the same individual before acclimatization.

Some physiological criteria of acceptable performance in the desert may at present consist in smallness of values of rectal temperature, of pulse rate, and of pulse pressure. These are the changes actually seen to occur during acclimatization.

In addition to criteria of this general sort, certain static characteristics of individuals are

recognized in part to be related to fitness. These are body build, high ratio of body surface to body mass, age, high density of active sweat glands, low resting pulse rate.

The theory is widespread that a man who is fit, is fit for almost everything. I find little evidence to support either this view or its alternative. In so far as much physical effort is called for, the many stresses and tests have much in common. If, however, physical work be deemphasized, then the man who is *fit* for the desert is, perhaps, as likely as not *unfit* for the tropics, for the arctic, for running, for flying.

Upon which of these possibilities is substantiated, depends the feasibility of dividing a whole population into groups fit for diverse climatic regions. Every individual can supposedly be helped to find for what environment he is most eminently fitted. Conceivably men will not be at the top or the bottom of *one* ladder of fitness, but each will perhaps be near the top in some one type of activity and environment. His natural endowments would then be put to the fullest use.

How test fitness? Every group of persons faced with the necessity of picking workers for the desert will have to assent to one or another series of final performances as criteria of desert fitness. The physiologist's task starts from that point; he devises tests whose scores are shown experimentally to be correlated (in diverse degrees) with those performances. Only by hypotheses does he make short work of his experiments if he is able to guess what tests will ultimately turn out to be decisive according to those criteria.

A test is a response to some standardized stress. The exact forms of test are multitude. Change of posture from lying to standing accelerates the pulse, raises the rectal temperature, and increases the systolic pressure. It is commonly agreed that those individuals in hot atmospheres who show least increment in each of these three measures, are the most fit. But the proof thereof is not very satisfactory. In cool atmospheres football stars often faint with prolong standing while physiology instructors do not (Mayerson). Hence this test by itself may not be accepted as a whole criterion of "general" fitness. Much the same results are found whether the standing is active, or passive by means of a tilt table.

The erect posture makes for poor return of venous blood. Not only the tensions in blood vessels are crucial, but also the tensions in muscles. Henderson *et al.* (1935) suggested that muscles reflexly maintain high tensions in response to cooling of the skin; a warm skin makes for relaxation and pools the blood peripherally. Heat alone might be insufficient to embarrass the circulation; but when heat and some other condition impinge together their effects are not merely additive (Gregory and Lee, 1935).

Work tests are of the same nature; instead of a postural change, movement is required. But here the circulation is in part promoted by the movement itself. In actual tests, fixed tasks are performed by walking, bicycling, stepping, or shovelling.

Dreosti (1935) had prospective miners repeat a standard shovelling test upon successive days in a chamber having air at 95°F and saturated with moisture. Some men had increases as great as four Fahrenheit degrees in oral temperature in one hour on the first day. Most of them had smaller increases each successive day, and after 4 days had apparently gained full tolerance to the heat. A few, however, showed little gain in tolerance even after one week. Thus the unfit were detected; they were thereupon kept out of the hot mine, after which the incidence of heat stroke fell to practically nothing. It is believed such repeated tests will sieve out those unfit for the desert; but no field results have been published so far.

Various forms of walking and stepping tests have been used, and some few correlations with field performances in heat have been drawn up. None serve to insure top performance, but they usually detect those men who will perform much below the average.

Like all empirical tests of physiological state, these "cardiovascular" tests ascertain some generalized response to specific circumstances. There is no evidence that a hundred other tests would not be equally useful. What one looks for in such a test is ease of use, small error of measurement, high correlation with ultimate performance, high variability among individuals, and low variability in the individual on different days. In general, however, it seems much better to rely upon more than one test, thereby increasing the predictive power and deemphasizing any one characteristic of the individual. I believe it is unlikely that any one test can be as decisive as several tests.

It seems possible that measurements of static traits of the individual, such as weight, vital capacity, and chest circumference, may be by themselves as useful indices to fitness as the measured responses to fixed stresses.

Comment. Evidently no *single* criterion of fitness is likely to be accepted, and no single test inform the physiologist of a man's ability to meet all criteria. By the same token, a psychologist's selection or a physician's selection cannot suffice for all purposes; there is a special role for the physiologist's appraisal of fitness. That appraisal may be based upon exact correlation of the same sort as that by which one predicts the rate of basal oxygen consumption from body size. It is to be established by the same sorts of exact measure-

ment, designed for the purpose, and analysed rigorously.

With the various tests available, can men be selected for life in the desert? No published results demonstrate whether selection can be successful or not. No single test or combination of tests has yet been specifically tried on a sufficient scale.

Can men be preselected for their ability to acclimatize? No one seems to know what relation exists between characteristics before exposure to heat and those after exposure. But the methods of finding the correlations are fully ready; they are the standard procedures for ascertaining coefficients of correlation between final performance and preliminary ratings.

How specific is fitness for the desert? Again, no one knows. But the methods of observing how far those that are fit for the desert are also fit for tropics or mountains belong to all physiologists. Nothing seems more fundamental to the understanding of man in relation to environment than to know which fitnesses conflict, and which ones reinforce one another. There is no evidence that high performance in the heat precludes high performance in the cold, or vice versa.

Of the various stresses that impinge upon man in the desert, many are to be met by intelligent use of *material aids*. Dust is countered by a dust mask, glare by goggles, infrared radiation by helmet and porous clothing, water and salt losses by doing everything possible to insure adequate supplies of water and salt.

So far air conditioning is not supplied in every vehicle and building. Yet in many ways "man is more indebted to the ingenuity of his mind than to the pliability of his body" (J. Johnson, 1821, p. 1). The factors for which no amount of thought can compensate are the "internal" ones, chief of which is probably maintenance of adequate blood circulation. After acclimatization has done its utmost for all men, those men who outlast others can be found by methods of the general sorts suggested. Hence most tests of fitness to be advocated have to do with circulatory factors. The same bodily system that appears to break down first in aviation, athletics, and most other endeavors, also limits most the man in the desert.

Physiological regulations involved. The stresses from rapid turnover of heat, of water and of salt, from glare and dust, put strains upon the various systems of that body. The responses to stresses are coordinated in accordance with the simultaneous demands for heat transport, water distribution, blood supply, and all the rest. I think it is plain that fitness is a manifestation of the regulatory capacities with respect to the many properties which the body is concerned to preserve.

The organism has means of preserving each of its properties in a consistent fashion (Adolph, 1943). Every time an excess of heat is present, losses of heat accelerate and gains of heat diminish when possible (by inhibition of extra heat production). When the body has a deficit of heat, heat losses are minimized and heat gains are accelerated. The heat content or body temperature that is preserved represents some common agreement among all the processes of heat gain and of heat losses. They strike a balance or equality of heat exchanges.

These processes of heat exchanges go into action with diverse provocations. The sensitivities to provocation vary among individuals; they are also the factors that vary in the same individual with successive exposures. The pattern of agreement among the processes has then shifted. But the capacities to become modified are also diverse. In the end, each of the several processes of heat loss turn out to be sufficiently varied that some men endure what others do not.

The diverse forms of physiological difficulty that hot climates bring to man are reviewed by Castellani (1938). The chief breakdown of regulation to which man is liable is heat exhaustion. The man is still producing sweat and keeping cool, but he may become utterly miserable, with rapid decreasing pulse and variable pulse pressure (Adolph, 1924; Weiner, 1938). Usually he needs merely to lie down in order to feel better. The shock-like circulatory failure appears to be the crucial element in his situation. If he is unacclimatized he can improve his lot by subjecting himself to heat more gradually. But if he is already acclimatized, there is much evidence that exhaustion will recur. He is one of the unfit.

Conclusion. Fitness is the suitability or preparedness of the human body for operating in a specified manner in prescribed surroundings. The climate of the desert is a series of forces acting upon the several regulatory systems of the body. The systems respond, within limits, to demands of the environment. The abilities to respond, whether inherent or acquired, can be sized up to a small extent from static traits of the body and to a large extent from arbitrary tests devised for the purpose. The specific tests still need to be developed and evaluated.

Many of the disadvantages to which the body is exposed in the desert, such as dust and glare, can be obviated by protective devices. Others, such as requirements of water and salt, can be met by the utmost ensurance of their adequate supply. Internal factors that limit performance in the desert appear to be chiefly circulatory. These factors are powerfully changed by acclimatization. After acclimatization has done all it can to improve the transport of blood, the only means of avoiding exhaustion in more extreme conditions is to select individuals who are fit. At present,

such individuals appear to occur at random; but there is some evidence that exposure to heat in infancy may enhance the abilities to compensate the stress of heat.

The purpose of this paper is to present certain problems of desert physiology that seem ripe for solution. If men are to live in the desert with all the advantages for enjoyment of it that can be put at their disposal, these problems must be answered. Not to seek the answers is to assume that every man can overcome the limitations of bodily capacity by sheer determination of will power. In reality, the fit man can be identified from among his fellows, and his operating characteristics can be appraised in the most rigorous engineering terms.

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PHYSICAL PERFORMANCE IN RELATION TO DIET

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There is at present a widespread belief that physical performance, particularly in industry and in the Armed Forces, is frequently limited because of nutritional inadequacies and that, in general, vigor and muscular ability can be improved by better diets and the use of special foods and food concentrates. The trend of thinking among nutritionists has been in the same direction (34) (51) (160) (159) (217) (228) (353). Where real deficiencies exist there is little question that physical performance is hindered; the real problem is what can be done by dietary measures to improve the performance of persons who are not clearly underfed or malnourished. The concrete facts which can be adduced are few; the relevant literature is voluminous but frequently unsatisfactory. The space allotted here would be insufficient to discuss only the fundamental theories —and familiarity with the field leads to distrust of facile reasoning at the present stage of knowledge. On the other hand, most of the current extravagant claims for various dietary measures have some real or supposed theoretical basis. Mere tabulation of the various claims and reports would be largely a compendium of irresponsible conclusions and the results of uncontrolled "experiments." The present treatment is a compromise in which an attempt is made to record the majority of reports which have some claim to the experimental approach together with indications of theoretical bases. The result is that the individual questions and articles are of necessity treated with the utmost brevity and critical judgments are often stated with little discussion. The synthesis of data to provide specific recommendations which are both practical and scientifically defensible must await new data and another occasion. Finally, the large subject of inanition and total caloric needs cannot be treated here.

Notes on theoretical aspects. The provision of food for the support of physical work is obviously

primarily for the purpose of supplying fuel to the working muscles. The belief that the kind and relative amounts of foods supplied makes an important difference is basic to all theories about diet and muscular performance. Some substances, such as glucose, are advocated because they are obviously combusted in muscles and they require a minimum of digestive and metabolic preparation for absorption and use. Substances like creatine, lecithin and phosphates are recommended because they are normally prominent in muscle and nervous tissue. Gelatin is urged because its contained glycine may be used in the formation of muscle creatine. On the other hand, fats are disdained because their use in muscle metabolism is apparently indirect. Alkalies are offered to counteract some of the changes which result from muscular exertion. Finally, realization of the participation of some vitamins in the enzyme systems of carbohydrate metabolism leads to the suggestion that an increase in the intake of these vitamins will facilitate the reactions involving these enzymes.

It is clear that the theories offered for aiding work performance by special dietaries generally attempt to maintain the muscle composition in its unfatigued state by:

1. Renewing the supply of energy-yielding substrates, or
2. Facilitating the energy-yielding reactions, or
3. Counteracting the physical-chemical changes accompanying the metabolic processes in the muscle.

The simple application of such theories is obstructed by the remarkable homeostasis of the animal organism and the fact that some of the changes accompanying muscle metabolism are protective or are part of a larger adaptive mechanism. This is not to decry the theoretical approach but merely to suggest that many of the theories offered are over-simplified and naive.

Criteria. The ideal criteria for the effect of a diet on work are those of actual performance under controlled conditions. These are very difficult to apply scientifically because of the formidable necessities in equipment, subjects and time and the difficulty of defining performance so that it is uninfluenced by extraneous factors. Simple tests of strength or work capacity in man are extraordinarily dependent on motivation. Skill, and the co-ordinated use of local muscle groups, is an important element in many "tests," in these tests training effects are so large that months may be needed to get reasonable standardization even in control experiments. Animal experiments are unsatisfactory because, though the general course of metabolism in man and animals may be similar, the quantitative relations are not identical and it is precisely the quantitative relations which are desired for practical application to man.

It is our belief that physical "fitness" and work capacity are best estimated by the imposition of standardized tasks which require a minimum of training and are within the capacity of the subject to perform. The effects on the body of performance of these tasks are then measured. The variables to be considered should be those which reflect the strain on the physiological functions (pulse rate, body temperature, stomach evacuation, reaction time, etc.) and the resulting distortion of the body chemistry (such as blood lactate, pyruvate, glucose, urea, etc.). The imposition of a second strain on top of that of the exercise may be useful; illustrations would be glucose tolerance or measured dehydration. In more chronic studies the maintenance of weight and of balance in nitrogen, minerals and other substances is important. All procedures and conditions must be rigidly standardized; this includes environmental conditions and the timing of all procedures. In all cases it is of the highest importance to recognize that human beings are extremely suggestible and their subjective statements and even objective appearance reflects irrelevant personal psychological matters more often than not.

These points are emphasized because their neglect has been responsible for the fact that the majority of "evidence" offered for the relation of diet to physical performance of man is of dubious character. Too often a regime for normal man is proposed on the basis of observations on patients in the clinic or the results of uncontrolled "trials." And recommendations based on results from acute experiments on animals can lead to serious error.

The fuels of muscular work. The demonstration by Pettenkofer and Voit, in 1866, (319) that nitrogen excretion is little affected by exercise disposed of Liebig's theory that protein is the fuel of muscular work. Since Chauveau, in 1896, reported a rise in R.Q. toward unity in exercise (83) it has been generally believed that carbohydrate metabolism is almost the sole source of energy for muscular contraction. However, Zuntz (410) and many subsequent workers reported that the R.Q. in work is very similar to the value in rest. Actually, Chauveau's finding applies to heavy work and that of Zuntz to light or moderate work (39) (68) (85) (89). Though carbohydrate metabolism is normally dominant in hard work we must now recognize that fats play an important role and that gluconeogenesis from protein is not necessarily inefficient. The difficulty in interpreting respiratory quotients is illustrated by the extreme values which are found with rats trained to abnormal eating habits (388).

It appears that, at any one time, the substances metabolized depend upon the relative availability

of substrates, the accumulation of metabolites, the intensity of work, and the amounts of various enzymes present. A change in dietary balance requires re-adjustment in the enzymes before a new balance is struck; in the meantime the course of metabolism may reflect the previous dietary balance for some days. The ideal dietary for muscular work cannot be estimated by brief experiments with highly abnormal diets. Until such time as relatively long-time studies can be made it is impossible to arrive at definite conclusions. Fortunately, the capacity of the human organism for adjustment is such that marked differences in the proximate composition of the diet are ordinarily attended only by small changes in energy metabolism and work performance is apparently largely independent of these. It may be, of course, that such differences assume critical importance in some situations involving unusual strains, such as very prolonged hard work or partial starvation. Theoretical speculation from the present data on intermediary metabolism is relatively profitless for practical application.

Frequency of meals. In general, both blood sugar and respiratory quotient rise shortly after a meal containing carbohydrate and then decline for several hours. These facts may be interpreted to mean that the availability and utilization of carbohydrate follow a corresponding time path. By shortening the periods between meals it is readily possible to smooth out these cyclic variations. If the simple theory is adopted that normally a limiting factor for work output is the supply of sugar to the tissues and that this is reflected by the blood sugar, then a theoretical argument could be made for efforts to maintain the blood sugar at a high level. Haggard and Greenberg appear to have accepted this theory and have pursued it to the logical conclusion of recommending frequent and between-meal feeding (170) (171) (172) (173) (190).

Cyclic rhythms in the blood sugar and liver glycogen are normal phenomena in man (239) and other animals (1). The liver glycogen cycle in the rat persists for a day of fasting and may be altered by changing the feeding periods but the new cycle requires about a week to be established (196) (197). The blood sugar cycle in the rat persists for 36 to 48 hours of starvation (321). These phenomena should be noted in discussing alterations in meal hours and periodicity.

It is probably true that our custom of 3 meals a day has developed because of convenience rather than because it represents the physiological optimum. The experience in industry seems to be favorable towards the provision of mid-morning and mid-afternoon rest periods during which food is taken. However, simple rest periods without food also appear to be beneficial in industry. Much of the discussion on this subject is properly in the province of psychology and will not be treated here. The reported effect of additional meals on absolute work efficiency is more pertinent. Haggard and Greenberg, in 1935, (171) claimed the consumption of a meal produced an increase in muscular efficiency of the order of 25 per cent. Alterations in efficiency of this magnitude are far out of line with all other observations (69) (72) (115) (154) and justify doubts about other items in the reports from the Yale laboratory. Repetitions of these experiments by Haldi, *et al.* (177) failed to give any confirmation for the reported effect of a meal on efficiency. No effect of sugar ingestion appears in simple work tests (73) (313). In prolonged exhausting exertion like marathon races glucose may be useful (62) (29). Such conditions, of course, never obtain in ordinary occupations.

Experience in this Laboratory would support the use of between-meal feeding when extremely hard work is being performed but does not indicate any such utility at more ordinary intensities. If the volume of production in factory operations is to be considered as the criterion it is possible that different conclusions would be drawn. The cause of the improvement produced by extra meals in factory output, however, cannot be ascribed only to simple physiological causes; probably boredom and employee-employer relations are much more importantly affected.

Sugars. Sugars are excellent fuels for immediate use in muscular work. A phenomenal output of continuous work can be produced by the dog if glucose is administered at frequent intervals (116). This does not mean that other sugars and more complex carbohydrates might not be similarly effective. The supposition that glucose ingestion renews the fuel for work with unique rapidity assumes that the hydrolysis of other carbohydrates makes an important time limitation. There is no proof that this is the case with disaccharides. Actually, the hydrolysis of sucrose in the digestive tract proceeds so rapidly that its contained glucose becomes available about as fast as it can be absorbed. The digestion of starch is more rapid than frequently believed, much of this taking place in the stomach (26).

Glucose is absorbed in some circumstances from the gut twice as fast as fructose (95) (261) (379) (392) but the difference decreases when large amounts of sugars are ingested (96) and, in general, absorption proceeds more rapidly than the muscles can use the absorbed sugar. There is little difference between glucose and fructose in the total amount of sugar absorbed in 2 or 3 hours or in their efficacy in restoring glycogen in fatigued muscles (308). The total amount of carbohydrate metabolized in exercise is not specifically affected by the

prior ingestion of either glucose or fructose but some of the fructose may be converted to fat and thus be less efficacious in conserving the bodily store of carbohydrate (16) (176). The estimation of utilization of the various sugars is complicated by the fact that the R.Q. rises above 1.0 after ingestion of sucrose, galactose, levulose or dihydroxyacetone (78); part of this effect is traceable to lactacidemia provoked by fructose (16) (66) (391).

The blood sugar in work is not a good indicator of carbohydrate metabolism or requirements in normal men and the course in work may be different in athletes than in untrained young men (42). The R.Q. in work frequently changes without like changes in blood sugar (88) (89) (97) (98) (266). This relative independence suggested the theory that fatigue in hypoglycemia arises from an effect in the central nervous system rather than from inadequate carbohydrate use in the muscles (42) (88). In opposition, we have found that as work continues in fasting the fatigue increases steadily though the blood sugar is constant for some hours, then declines to very low values and finally rises to intermediate levels (see "Frequency of Meals").

Proteins. Muscular work is followed by a very slight increase in nitrogen excretion which continues for 24 to 36 hours (75) (76) (152). There is no close parallelism between the amount of work and the excess nitrogen excretion (398). On the third day after hard work the nitrogen excretion falls below the basal level (399). These facts certainly do not indicate any need for extra protein in hard work. Many people efficiently carry on hard work for years on very low protein intakes (365). It has been reported that creatine phosphate in muscle is increased on a low protein diet and decreased on a meat diet (299). The fact that few athletes are vegetarians (387) has no special pertinence here. Both high (123) and low (90) (295) protein intakes are recommended for athletes on equally slight grounds. In a vegetarian cyclist Wishart, in 1934, (400) found higher gross efficiencies on a low protein diet but better endurance when the protein intake was 200 or more grams per day.

Naturally, the protein intake must be adequate in amount and in essential amino acids to maintain balance. This would be readily achieved with an intake of 40 or 50 grams of protein a day. Additional protein may be desirable to build up a reserve of labile body protein for emergencies (389). On reasonably good diets such stores are increased by extra food, including proteins (107) (104). A high carbohydrate meal taken before work has a sparing effect on nitrogen excretion during and after the work (105). In some practical situations with long periods between meals the relatively slow digestion and absorption of proteinaceous foods might be an advantage.

Fats. For a long time fats have been held in low esteem as fuel for muscular activity. Diets high in fats are tolerated poorly and provoke ketosis; on the other hand diets very low in fats generally produce no obvious symptoms though minimal amounts of certain fatty acids are essential to health (59) (63) (64) (65) (137) (377).

A few early experiments indicated that muscular efficiency is reduced (148) (6) or unchanged (27) on a high fat diet. Krogh and Lindhard, in 1920, (241) put the question on a much sounder basis. They found that subjects maintained on a high fat diet showed a smaller net muscular efficiency than when they were on a high carbohydrate diet. By plotting R.Q. against net efficiency, extrapolation to pure fat metabolism (R.Q. of 0.70) indicated 11 per cent greater energy expenditure per unit of work than for pure carbohydrate metabolism (R.Q. of 1.0). Careful repetition of these studies gave an average difference of 8.3 per cent in efficiency on the two fuels (32). Qualitative confirmation was also obtained by others (38) (48) (268). Dogs expended 6.7 per cent more calories per unit work after fat ingestion than after glucose ingestion (327). The report of decreased spontaneous activity on a fat diet (318) is suggestive only. The study of Cathcart and Burnett (76) only partially confirmed Krogh and Lindhard but the diets used were not very extreme. Other negative results (334) were based on inadequate observations and experiments.

Gemmill's (154) criticism of the extrapolation method used by the Danish school cannot affect the general thesis. The difficulty of obtaining precise numerical results for comparison is evident in the work of Christensen and Hansen (87), where training effects as well as vitamin and protein limitations may have interfered. They interpreted their results to support Krogh and Lindhard and, in any case, they clearly showed that endurance is much less on a high fat diet; at oxygen consumptions of 2.4 to 2.9 liters per minute the men could continue 2 to 3 times as long after the high carbohydrate diet than after the high fat diet. Caution must be observed in applying these results to other situations. The high fat diet used was extreme (95 per cent of calories from fat) and the "endurance" was at most only a matter of a few hours.

The cause for decreased efficiency on fat is conjectural. When fats are used to supply almost all the energy their combustion may proceed through inefficient reactions (35) (36). Complete energy balance studies over some days would be needed to settle this point.

Christensen and Hansen (87) suggest the lack of endurance on the fat diet may be due to ketones in the blood or to the effect on the central nervous system of the low blood sugar level (42). However, there is no evidence that ketonemia *per se* is deleterious; actually ketones are readily used as a

fuel. The blood sugar argument fails to explain how fatigue may become more marked in the face of a rising level of sugar in the blood; we have found this condition when hard work without food is continued for several days.

Whether the diet is high or low in fat, the continuance of work without food produces a fall in the respiratory quotient and eventually an accumulation of ketones in the blood. These ketone bodies are capable of utilization for muscular work at a rate which bears some proportionality to their concentration in the blood (36) (125) (183) (302) (301) (374) (390). The idea that, functionally at least, ketone bodies can take the place of glucose in muscle metabolism can be argued (100). In marked ketonemia (80 mg. per 100 cc. of blood) Wick and Drury (390) calculated that the metabolism of β-hydroxybutyric acid would account for 85 to 90 per cent of the total oxygen usage of the rabbit. They suggest that the formation of ketone bodies "may be considered analogous to the conversion in the liver of amino acids to glucose for utilization by the tissues". When ketosis is produced in guinea pigs by fasting there is less depletion of carbohydrate stores in subsequent work than when the pigs are fed; these differences are ot reflected in different endurance on the treadmill (302).

The evidence cited indicates that ketosis in normal persons is hardly as deleterious as is sometimes imagined from experience with diabetic acidosis. In the energy metabolism of fats the scale of preference would seem to be: ketone bodies, hort chain fatty acids and finally long chain fatty acids (251). "Depot fat" probably cannot be used directly but it is hardly a metabolic "dead end". The phospholipids likewise do not seem to be directly concerned in muscle metabolism (357), though their exchanges are affected by muscular activity (149).

The long-standing controversy about gluconeogenesis from fat has been reviewed by Soskin (360); opposing arguments were given by Cori (96). There is increasing evidence in support of the view that fat may supply sugar (153) (407) (360).

Much more work on fat metabolism is needed to answer some practical questions. Fatty foods, because of their concentration and resistance to freezing, would seem to be ideal for winter and arctic warfare but the metabolic consequences must be discovered. One danger is that long-continued fat diets may produce liver cirrhosis (81). In the absence of better information we must conclude that at present it is unwise to allow the percentage of calories in the diet derived from fat to go much above 50 per cent. If a single fat is to be used in excess, butter may be preferable to some other common fats (336). Further, it may be unwise to make sudden changes in the fat-carbohydrate ratio. After a high fat diet it takes several days before a high carbohydrate diet can again be properly utilized (310).

The vitamins—General remarks. The capacity to perform physical work is obviously hindered by the development of frank vitamin deficiency states. Muscular weakness, incoordination and apathy are outstanding characteristics of advanced beri-beri, scurvy and pellagra. Discussion of these conditions has no place here but questions of vitamin "supercharging" and of "sub-clinical" deficiencies are important. The problems involve the differentiation between ordinary "health" and "abundant health", with the presumptive connotation of ordinary and of unusual work capacities.

Thiamin, riboflavin and nicotinic acid function in enzyme systems which are fundamental to energy metabolism. The beautiful studies on these points, however, do not answer the question as to the extent to which muscular function is normally limited by the amounts of these enzymes available in the intact animal. Similarly the researches on the biochemical roles of vitamin A and of ascorbic acid do not in themselves prove there is any utility to increasing the intakes of these vitamins beyond the amounts needed to prevent definite abnormalities. Opinions on these points are not wanting; critical data, though rapidly accumulating, are still limited. Finally, there are questions as to how long restricted intakes of the several vitamins may be endured before there is an adverse effect on work performance.

Vitamin A. There is little evidence that muscular function has any direct and immediate relation to vitamin A intake. Drigalski (124) reported that a healthy man developed easy fatigability and muscular cramps after several months on a diet very low in vitamin A but there were no objective controls. Guerrant, Dutcher and Chornock (167) reported that rats on a diet supplemented with extra vitamin A showed more spontaneous activity than controls and that exercise delays the appearance of vitamin A deficiency. The interpretation of these findings is obscure. Wald, Brouha and Johnson (383) found that human subjects showed no decrease in fitness for physical work after 6 months on a diet extremely low in vitamin A. This result may have been complicated by the fact that the subjects had previously been on a regime of very high vitamin A intake; the fact that vitamin A did not disappear from the plasma in those subjects indicates that their reserves were far from exhausted. The depletion of vitamin A stores in the body takes a very long time so that there is a substantial margin of safety in this vitamin in most cases. Vitamin A disappeared from the blood of dogs in 5 months on a diet almost free of vitamin A; 10 months later there were still traces in the liver (247). These dogs remained in apparently

normal health and activity throughout. The muscular dystrophy occasionally seen in rats on diets deficient in vitamin A is probably due to an associated deficiency in vitamin E (238).

Human performance may be restricted by lack of vitamin A because of effects on vision. Defective dark adaptation can be a serious handicap, notably in military operations. The use of liver in the treatment of night blindness was recommended by the ancients and the modern investigations on the subject constitute an outstanding development (382). However, the relation between night blindness and vitamin A intake is by no means as direct as appeared to be the case a few years ago. Many persons can subsist for many weeks or months on diets very low in vitamin A before significant effects on night vision appear (109) (329) (383) (385). In other persons signs of defective night vision occur in a few days on a similar regime (124) (186) (384). In general, persons who quickly develop night blindness on a low vitamin A intake require prolonged treatment—up to some months —with large doses of vitamin A (258) (264). Other persons are greatly improved or even "cured" within a few hours after receiving large amounts of vitamin A, β carotene or cod liver oil (43) (212) (249) (384). Some of these individual variations must depend on differences in the stores of the vitamin in the body. There are suggestions that dark adaptation is not a very sensitive index of vitamin A nutrition (40) (208) (361).

By no means all cases of night blindness are due to simple deficiency of vitamin A in the diet. A third of the persons with poor night vision observed in Labrador were apparently not deficient in vitamin A (363). A careful study of 52 night-blind soldiers in England showed that a nutritional deficiency in vitamin A was not responsible; psychological factors were believed to be important (402).

Among "normal" persons subsisting on diets adequate or not markedly deficient in vitamin A there is little relation between vitamin A intake, blood vitamin A, and dark adaptation (23) (79) (362) (175). Attempts to produce unusually good night vision by large intakes of vitamin A have yielded negative results. There would seem to be little basis for recommendations that aviators should receive not less than 10,000 I.U. of vitamin A daily (31A).

Effects of vitamin A intake on color vision have been claimed and, if true, would affect human performance in certain occupations. The daily administration of carotene to factory workers was followed by a 75 per cent reduction in the number of rejections for off-color parts of stoves assembled by them (401). Altered color fields as well as night blindness were produced in 6 to 7 months on an A-deficient diet, according to Rauh (329). Dunlap and Loken (120) (121) (122) claimed that up to 80 per cent of persons with defective color vision were able to pass the color tests after a few weeks on a daily intake of 25,000 I.U. of vitamin A. Murray (296) expressed skepticism about these results. Extensive studies on R.O.T.C. students completely failed to confirm the idea that vitamin A can cure defective color vision (130). Not a single person of 41 men with poor color vision was improved by 25,000 I.U. of vitamin A daily for a period of 8 weeks.

Vitamins of the B complex. There have been numerous claims that supplements of vitamins of the B complex improve work performance and capacity even when there are no signs of deficiencies in these vitamins (103) (119) (162) (285) (294). Most of these are based on inadequate data without controls and may be dismissed at once.

The administration of yeast may promote some deposition of glycogen in the liver (30) but repetitions of the dosage have no further effect (320) and the glycogen storage is not influenced by yeast when sufficient carbohydrate is given (2). Thiamin, riboflavin, pantothenic acid and pyridoxine all promote glycogen formation in animals deficient in these vitamins (366) but large doses of thiamin may cause a decline in liver glycogen in normal animals (286). In any case the relation between liver glycogen and work performance is obscure. Sudden elevation of thiamin intake may cause liver damage (133). Reports that the work capacity of muscle is improved by thiamin injections (281) (178) are unconvincing. The claim that isolated muscles treated with thiamin become more responsive to acetylcholine (56) was shown to be in error by Kaiser (220).

Careful studies in this Laboratory failed to disclose any benefit on work performance or capacity from large daily supplements of the B vitamins given to soldiers maintained on ordinary U. S. Army Garrison Rations (226A). The general nature of these findings has been confirmed (356). The tests covered brief (anerobic) work, endurance, strength, psychomotor functions and details of metabolism which might be significant—blood lactate, pyruvate, hemoglobin, glucose, etc. As a matter of fact, normal young men may be maintained for at least several months on rations supplying only about 0.25 mg. of thiamin per 1,000 Calories with no adverse effects in these variables compared with very much larger intakes of vitamin B_1 (227). There are other indications that the margin of safety on thiamin and riboflavin provided in the Recommendations of the National Research Council (300) may be very large (202) (243). Limited body reserves of thiamin may be established by extra thiamin feeding but the riboflavin and niacin stores are not much affected

by the intake of those vitamins beyond the minimal level (343). Reports that an intake of riboflavin which appears adequate for growth and reproduction may be sub-optimal in more than one generation (131) cannot be discussed here.

It would seem that there is at present no basis for high supplementation with vitamins of the B complex to promote better work performance. The requirement for thiamin is probably proportional to the intensity of the metabolism (99) (168) though this relation has not been proved yet in man. A similar relation between metabolism and requirement is assumed for riboflavin and niacin on rather slender evidence. It is entirely justifiable to advise an increased intake of B vitamins when work is increased. With a reasonably good diet this is guaranteed by simply increasing the total food eaten.

There are many emergencies in war when drastic dietary alterations occur. The question as to the rate at which a deficiency in B vitamins becomes limiting to work performance is important. It has been claimed that when very small amounts of thiamin—0.5 mg. or less daily—are provided symptoms of deficiency appear within a few days (217A) but these reports cannot be accepted. When proper controls are provided no significant symptoms occur for some weeks or months (243) (385A) (395) (396).

Recently claims have been made that a diet deficient in B vitamins produces some physical deterioration in 4 weeks in sedentary men and marked reduction in work capacity within a few days in men doing hard work (127) (213). After careful consideration these claims must be rejected in toto. We may note that in the work cited the intake of neither vitamins nor calories nor the output of work were measured, that none of the results were reported in full, that the subjects were highly conditioned to expect deterioration, that controls or allowances for training effects and over-exertion were not made, that the only sure deficiency in the diet was in thiamin, and that the subjects who received extra thiamin also showed "symptoms". We have repeated this work with a still more restricted diet applied twice as long, with exact measurement of intakes and work output, with proper controls and with objective measurements of physiological, psychomotor, psychological and biochemical variables in rest, in different types of work and in recovery (243). The detailed results will be reported elsewhere; they completely negate the claims that important effects on work performance occur in a few days or weeks when normal young men do very hard work while subsisting on a diet severely restricted in the vitamins of the B complex.

Space does not permit discussion of the possible protective effects of extra B vitamins in occupations involving exposure to toxic materials, excessive light, or emotional strain. Claims for higher requirements in hot environments (279) (278) (280) (284) are unconvincing and we have found no utility of extra B vitamins for hard work in periods up to a week at extreme heat (191A). There is no significant loss of thiamin or riboflavin in sweat though there may be an appreciable loss of niacin (179) (275) (358) (369). The claims made for pyridoxine in neuromuscular disorders are based on clinical impressions (8) (18) (215) (216) and have been denied (112) (118) (140).

Ascorbic acid. Like other vitamins, ascorbic acid has been suggested for increasing work performance. Benefits in rats from ascorbic acid injections have been claimed (17) and denied (52). Generally positive but quantitatively discordant results were reported for isolated frog muscles when ascorbic acid was added to the medium (21) (33) (166) (354) (381). Perfused frog muscles show no increase in work performance when ascorbic acid is added to the perfusing fluid (4). The ascorbic acid content of rabbit muscles is said to be increased by training and reduced by fatigue (236) (350). The fact that scorbutic muscle fatigues rapidly (328) is not surprising.

Claims for benefits of ascorbic acid on work capacity of persons who show no signs of clinical scurvy (22) (60) (285) are not based on acceptable evidence. South African mine workers, who were on a diet markedly below ordinary standards for vitamin C, showed no gain in work capacity or performance when they received daily supplements of vitamin C (91) (214). Fox and Dangerfield (146) have collected much evidence to show that the performance of Bantu laborers is substantially the same for months at 25 and at 50 or more mg. of ascorbic acid daily. In this Laboratory we found that muscular performance is not affected in any way by the addition of 200 mg. of ascorbic acid daily to U. S. Army Garrison Rations containing about 70 mg. (226A). Studies on intermediary metabolism and blood chemistry in rest, exercise and recovery were likewise entirely negative.

Extreme deficiency of ascorbic acid intake can be tolerated by man for a surprising length of time. Rietschel and Mensching (337) maintained a normal man for 160 days on a diet free from vitamin C. There was no loss of weight at any time and no symptoms of any kind for 120 days. Similar results were obtained in an almost identical experiment by Crandon and coworkers (101) (102). In their subject the plasma was free of ascorbic acid in 44 days but beginning signs of scurvy were not seen for 5 months (101) (102) (253). In these studies clear signs of a reduction in work capacity were not seen though some lethargy was noted.

It has been claimed that the requirement for

ascorbic acid is increased in hard work in the heat (7) (28) (201) (280) partly because of loss of vitamin C in the sweat (28) (96A). Subsequent work indicated little ascorbic acid in sweat (179) (409) (406) and the most careful work indicates that sweat actually is almost completely devoid of vitamin C (275) (369).

Reports of benefits of ascorbic acid supplementation in industry in hot environments (7) (201) have not provided detailed data. In this Laboratory we have made extensive controlled studies covering periods up to a week at hard work in temperatures up to 122°F. These have completely failed to demonstrate any effect of ascorbic acid intake from 40 to 540 mg. daily on work performance, endurance, psychomotor ability or the incidence of heat exhaustion (191).

Vitamin E. Nutritional muscular dystrophy and tissue changes produced by a deficiency of vitamin E have been reviewed recently by Pappenheimer (314) and by Wolbach and Bessey (404). Evans and Burr (135) produced muscular weakness and paralysis in rats on a diet deficient in vitamin E. Similar effects have not been found in man but have been recorded in rabbits and guinea pigs (158), ducks (316), sheep and goats (262) the tree kangaroo (161), mice (315) and hamsters (207). Pups born of vitamin E-deficient mothers show signs of muscular lesions (5). Dogs with chronic biliary fistulae develop muscular defects which have been ascribed to faulty absorption of vitamin E from the gut (57).

The addition of cod liver oil to a diet deficient in vitamin E intensifies the development of nutritional muscular dystrophy (262). The mechanism responsible is still debatable but rancid oils favor the destruction of vitamin E in the intestine and may therefore aggravate a deficiency (270).

Vitamin E deficiency in susceptible animals produces alterations in the central nervous system and extensive necrosis in the voluntary muscles (129) (136) (311). The muscles of these animals show increased rheobase and chronaxie (380) and reduction in contractile ability; the latter change can be demonstrated before the animal shows gross outward signs of weakness (232). These alterations are reversible by the administration of vitamin E or synthetic dl-alpha-tocopherol (233).

There have been numerous studies on the chemical composition of the dystrophic muscles. These reveal the alterations expected in view of the atrophy and necrosis but there are few definite signs of a specific chemical defect in minerals (138) (139) (288), phosphorus compounds (156) (252) (289) (290) (291), or lipids (292). The creatine content of the muscles is decreased and creatinuria develops (155) (289) (290) (291) (306) (378), (cf. section on "Creatine").

Dystrophic muscle is characterized by a very high resting oxygen consumption and this abnormality appears at the stage where muscular weakness is marked but before there is severe paralysis (150) (380). The oxygen consumption quickly returns toward normal in the presence of alpha-tocopherol (207) (224). Evidence is inconclusive as to whether these effects are to be referred to the simple anti-oxidant action of vitamin E or whether, as Houchin and Mattill (207) suggest, vitamin E participates more directly in the metabolic processes.

Vitamin E has been suggested for the treatment of human neuro-muscular disorders and weakness but there is no adequate basis for such recommendations (126) (181) (351). Most of the interest has been directed toward pronounced and specific pathologies such as progressive muscular dystrophy, bulbar paralysis and amyotrophic lateral sclerosis (31) (169) (364) (386) (405). Vitamin E is suggested in the treatment of muscular atrophy resulting from polio-myelitis (352).

At present it cannot be concluded that vitamin E plays any direct and important role in neuromuscular function of normal man. Species differences are important; chicks only exceptionally develop muscular disorders on a diet almost free from vitamin E (314).

Acidosis and alkalosis. Dietary peculiarities are capable of producing moderate alterations in the alkaline reserve in normal persons but studies on the possible effects of acidosis or alkalosis on muscular performance have generally involved more drastic means, such as the production of acidosis by the ingestion of ammonium chloride. As usual, it is necessary to differentiate between simple acidemia in which the pH is lowered and acidosis in which the alkaline reserve is lowered. The fact that severe muscular work produces fixed acids which lower both pH and alkaline reserve has long encouraged the belief that alkalizing regimes are beneficial for the performance of exercise.

The accumulation of lactate in the blood is greater when the alkaline reserve is high (113) (114) (184). Accordingly, if the amount of lactate accumulated at a given level of work is taken as a measure of fatigue, it would be concluded that initial alkalosis is harmful. On the other hand it is perhaps more correctly argued that extra alkaline reserve allows more prompt and complete neutralization of lactic acid as formed and hence the higher level of lactate is an indication of better neutralization. Kaunitz and Selzer (222) suggested that lactic acid may actually delay fatigue. It should be obvious that predictions of performance cannot be made from such theoretical arguments. The conclusion of Dennig, *et al.* (113) that acidosis produced by ingestion of ammonium chloride reduces physical efficiency is based on measure-

ments of respiration volume and blood composition and is not supported by acceptable proof of an effect on actual work performance; the same is true of their suggestion that sodium bicarbonate ingestion increased physical efficiency. The latter claim has been denied (317). It has been suggested that the endurance of dogs may be reduced in alkalosis (348).

All work on this subject reported so far has been limited to rather acute and violent changes. Undoubtedly full adjustment to a condition of acidosis or alkalosis requires many days if not weeks. Practical conclusions cannot be drawn until prolonged experiments are made with moderate alterations in the acid-base balance. In the meantime the indications are that such changes in the alkaline reserve as may result from dietary alterations have little effect on ability of normal persons to perform muscular work. This conclusion is only tentative; the requisite data for more definite conclusions are yet to be gathered. The possible effect of the alkaline reserve on ability to work under conditions of partial or complete inanition should be explored further. Schlutz, Hastings and Morse (347) found, in dogs, that the rise in fixed acids in the body resulting from exertion is considerably more pronounced when the animals are on half rations. Acidosis tends to suppress ketonemia while alkalosis has the opposite effect. Associated with this effect we should note that urinary output of nitrogen and sulphur is augmented by acidosis while the liver glycogen is increased (260).

Phosphates. During the first World War Embden managed to convince the German military authorities that his ideas about phosphates and carbohydrate in muscle metabolism might be of practical use. He advocated foods and drinks rich in phosphate and in 1917 trials were carried out with acid sodium phosphate, first on a laboratory scale and then with whole battalions of soldiers in the field. The basic idea was that muscular performance depends ultimately upon the supply in the muscle of a basic energy substance—Embden's "Lactacidogen"—and that if the supply of this could be increased there would be an improvement in performance. Direct administration of lactacidogen, or hexose phosphate, was recognized as impracticable but: "eine Erleichterung und Beschleunigung der Lactacidogen synthese konnte aber vielleicht durch Zufuhr von dessen uns bekannten Bausteinen, nämlich von Zucker und Phosphorsäure erzielt werden" (132; p. 68).

Embden and his colleagues were enthusiastic about their results though they admitted some secondary problems such as occasional cases of diarrhea and some difficulty in regulating the dosage. Trials with police officers were considered to be confirmatory and phosphates were widely used thereafter in Germany by athletes and for all sorts of fatigue and debility (11) (193) (194) (195). Though the evidence of benefit was scarcely unexceptionable, opposing reports have been based on even less solid grounds (143).

The specific claim that fewer calories are expended for the same work on days when sizable amounts of phosphate and sugar are taken than on control days (199) has been convincingly denied (335) (368). Numerous other reports claim that subjects on a high phosphate regime feel better and suffer less fatigue from work, but these provide little acceptable data (107A) (223) (322) (323) and may be set off against denials based on experiments that are scarcely more acceptable (265) (326) (349). At least it appears that the daily ingestion of large amounts of phosphate can be maintained for years with little harm (322).

In 1935 a series of papers from Krestownikoff's laboratory in Leningrad reported a variety of effects from the use of phosphates but the actual experiments cited would justify few conclusions. It was claimed (325) that phosphates improve psychomotor performance during recovery following muscular work and that pulse rate, both in work and in recovery, tends to be higher when phosphates are ingested an hour or so before one hour of moderately hard work (240). Further, skin temperatures in work were stated to be higher after phosphates (235); this was supposed to agree with the finding of a reduction in sweat production (108). Finally, it was concluded that the increase in chronaxie resulting from work is less when phosphate is taken and that the benefit of the phosphate appeared in measurements with Mosso's ergograph (245). In general, the Russian school stated that 1 to 3 grams of acid sodium phosphate (by mouth) an hour or so before work is effective but that 5 to 10 grams taken 9 or 10 hours before work is not. If the Russian reports are acceptable they would indicate that a simple increase in the phosphate in the diet would have little effect.

Freeman's (147) experiments with hexose phosphate in perfusion media used with frogs' hearts have been cited in support of Embden's theory but the few data offered are capable of various interpretations. The same may be said of the numerous and controversial reports on phosphate balance and excretion during and after muscular exertion (367).

Atzler and his colleagues (11) studied 4 subjects and 3 dogs over a period of some months and concluded that phosphates are beneficial. In this work the method for estimating work capacity is of dubious interpretation. In any case the results suggest that only one of the subjects derived appreciable benefit from phosphates and even in this case the control is unsatisfactory. Later studies with dogs by the same group add little to

the picture. Morse (293) studied the endurance of dogs on a treadmill and found no effect of phosphates. The most recent work on this subject seems to be that of Sauser-Hall (344) on Swiss soldiers in training and during convalescence from influenza. No data are given in scientific support of enthusiastic claims for "C-Phos"—a proprietary organic phosphate.

In summary, there is every reason to agree with Bøje's (41) skepticism of any effect of high phosphate intake on muscular performance. There is a high degree of unanimity of opinion that an acid phosphate drink tends to produce some exhilaration in many people but what its effect, if any, may be on fatigue and capacity for work is not yet clear. We may well believe that a diet deficient in phosphate would eventually lead to serious disorder. With all ordinary diets, however, such danger should be remote for adults.

Minerals other than phosphorus. The excitability and work capacity of isolated muscles are notoriously sensitive to the mineral ions in the internal environment. In the large literature on the role of potassium in muscular contraction (138) there are few evidences for an importance of dietary potassium on muscular work in normal men, however. When animals are maintained on a very low potassium intake the muscle potassium decreases and this decrease is accentuated by sodium salts in the diet (134) (192). Similar events are indicated in man from studies on potassium balance (394). No striking changes in muscle function were observed in rats in which much of the muscle potassium had been replaced by sodium by dietary means (192), and no harmful effects were seen in rats maintained on a potassium intake many times the normal level (277). Studies on work capacity are lacking in these conditions.

These findings may seem surprising when it is noted that in excised muscles small increases in potassium cause definite decreases in chronaxie (244) and in rheobase (82). Nothmann and Wagner (307) reported that the excitability of human muscles to electrical stimuli is increased by ingestion of potassium but not of sodium salts. Myotonic muscles are unusually sensitive to potassium alterations (58).

It is probable that changes in muscle excitability are produced by changes in potassium rather than by the absolute level of this ion. The exchanges of potassium across the muscle cell membranes as related to exercise are of much interest but their application to the problem of optimal dietary potassium for the intact animal is by no means clear. That exercised muscles lose potassium in fatigue is well known. Measurements with the isotope K^{42} show a great increase in potassium exchanges in both directions when the muscle is stimulated (174). Potassium penetration into muscle is increased by denervation (255).

A striking instance of the effect of dietary sodium and potassium on ability to work is seen in Addison's disease. A diet high in sodium and low in potassium is very beneficial but although such a regime increases the work capacity of adrenalectomized rats they are still inferior to the normal rat (209).

Few conclusions can be drawn as to optimum amounts of sodium and potassium in the diet. A high potassium diet is apparently not harmful except in Addison's disease and may be beneficial in familial periodic paralysis (151). Excesses of both sodium and potassium are rapidly excreted by the kidneys so it would seem that the best diet would be one that would err slightly in providing ample amounts of these minerals. The chloride intake is more critical. If there is free access to salt there seems to be little danger of chloride depletion even in hard work in hot weather but this rule does not hold when food is not eaten. In this Laboratory we have found that work capacity in the heat is greatly reduced when salt is severely restricted even when this does not involve the intervention of heat cramps or heat hyperpyrexia. The lower level of safety is a total intake of about 2 to 3 grams of NaCl for every liter of sweat lost.

Very high or very low chloride intakes may lead to substantial parallel alterations in oxygen consumption in man (74) and dogs (110). These changes can be produced by diet and can be observed in the eviscerated animal as well as in the intact dog (92). No clear effects are seen with serum chloride variations within ±5 per cent of the average normal value (92). The efficiency of the kidney is such that drastic dietary changes would be required to produce significant effects in normal men.

Recently it has been claimed that the daily ingestion of calcium gluconate expedites the recovery from exercise (269), but no convincing data have been presented. It goes without saying that in the long run the diet must provide enough calcium, magnesium, iron and other essential minerals to maintain balance in these substances. How much of a surplus is desirable to allow maximal muscular performance is unknown. It is frequently assumed that a diet high in iron will promote hemoglobin formation and that a high level of hemoglobin is beneficial for the performance of hard work. In normal persons this is doubtful except at high altitudes. In extensive measurements of the hemoglobin concentration in the blood of normal young men we have found that, in general, athletes tend to have *lower* levels than men less able to carry out strenuous exertion.

Creatine, glycine and gelatin. In recent years there has been much popular interest in the use of

glycine (aminoacetic acid) to increase muscular power and endurance. Gelatin, which averages about 25 per cent glycine, has been widely sold for this purpose. The basic idea has been to promote endogenous creatine formation, presumably to enhance the supply of phosphocreatine in the muscles. The hydrolysis of phosphocreatine to creatine and phosphoric acid is an important energy-yielding reaction in muscle activity and there is a well-marked escape of creatine from the fatigued muscle (128) (371).

Creatine is seldom excreted by the normal adult man unless large amounts are administered. In contrast, patients with muscular dystrophy and some other myopathies characterized by weakness frequently excrete large amounts of creatine (257) (211) (61) and the muscle tissue has a decreased content of creatine and phosphocreatine (93) (111) (200) (303) (332). Nutritional muscular dystrophy likewise is associated with an abnormal creatine metabolism (157) (136) (205) (206) (289) (291). Denervated muscles also show a diminution in creatine content parallel to the degree of atrophy but the actual concentration of creatine in the fibres is little affected (15) (77) (84) (198).

In normal men creatinuria has been reported in fatigue but this is not a characteristic phenomenon. Muscular training does not produce an increase in the concentration of creatine in the muscles (234) (242) (267) (274).

Beard (24) has claimed that muscle creatine is increased when creatine is administered but such increase is small at most (298). If it is desired to increase endogenous creatine it would seem more hopeful to supply natural precursors to creatine. The long-standing belief that glycine is a precursor to creatine in the body has been confirmed recently (37).

In studies on precursors to creatine, Brand and his colleagues (54) found that the administration of glycine to patients with muscular dystrophy produced a marked increase in their creatinuria. In confirming this fact it was reported that the patients were actually benefited by this treatment (276) (370). A large clinical literature has since accumulated on the subject.

Therapeutic benefits from glycine in muscular dystrophy have been alternately claimed (9) (24) (106) (237) (376) and denied (19) (53) (272). Histological and biochemical improvement without any corresponding gain in strength and endurance may occur (331) (332). The balance of evidence favors Nevin's (303) conclusion that occasional patients with muscular dystrophy are benefited by glycine.

The use of glycine in myasthenia gravis is of more dubious utility than in muscular dystrophy. In the latter disease there may be a demonstrable biochemical defect but in myasthenia gravis the only clear defect is in function (303) (225). The report that creatinuria and diminished muscle creatine occurs in this condition has not been confirmed. However, Boothby (44) (45) (49) and others (337) (376) reported clinical improvement of varying degree in myasthenia gravis. In spite of widespread trials these reports have not been confirmed. Myasthenia gravis is characterized by spontaneous remissions and there is reason for the conclusion that glycine probably has no place in its treatment (303). A report of improvement in work capacity from glycine in 2 cases of adiposa dolorosa (403) is not substantiated by objective data.

Consideration of the foregoing offers small basis for the promotion of strength and endurance by attempting to increase the creatine supply in normal muscles. In reality there are several questions. In the first place it has been seriously doubted whether the creatine content of muscle can be increased in normal persons. Rose (340) concluded that creatine formation cannot be increased by amino acids beyond the physiological needs of the cells. Beard and Pizzolato (24) (25) have reported that many substances including glycine and some other amino acids will enhance creatine formation. These statements have been challenged (37) (141) (142). Fisher and Wilhelmi (142) found that glycine injections in rats and perfusions of rabbits' hearts with glycine solutions failed to show any synthesis of creatine in the muscle tissue. Horvath (203) (204) carefully studied the effect of gelatin administration on the composition of the rat gastrocnemius and found it to be entirely without effect not only on creatine but also on creatine phosphate, hexose phosphate, total nitrogen, glycogen and adenosine triphosphate.

A second question is whether there would be any advantage to the normal muscle if its content of creatine could be increased. We have already recorded our doubts on this score. A third question is whether a small biochemical advantage in the fuel content of the muscle would necessarily be reflected in appreciably better performance by the intact organism. There is no evidence from other sources that the fuel supply in a muscle is the limiting factor in ordinary muscular work. The advantages of glycine have been claimed almost entirely in brief muscular work where final exhaustion of the fuel supply is not involved. The possibility that in some rare diseases creatine deficiency is observed in parallel with muscle weakness is no answer to these questions.

There remain the reports of direct trials and observations on the effect of glycine and gelatin on fatigue in normal individuals. The suggestion that glycine improves muscular performance and

reduces fatigue in such persons on normal diets was put forth by Boothby (46) but the early interest (189) (259) subsided. The subject was revived by the remarkable claims for gelatin reported by Ray, Johnson and Taylor (330) from bicycle ergometer tests on young men. Still more astonishing "benefit" was reported by Kaczmarek (218) (219) from similar trials. Kaczmarek added the report that equal work was accomplished at slower pulse rates. Prior and Knapp (324) obtained insignificant results in 70 girls. These reports did not present acceptable measurements or controls and exhibited internal errors and discrepancies.

A more elaborate series of studies was carried out by Beard (24) on the bicycle ergometer. Beard reported for one group of subjects that 5 to 12 grams of glycine daily resulted in an average increase in the rate of maximal work output of 22 per cent in women and 32 per cent in men, whereas Ray, *et al.* (330) had reported women receive no benefit. In a second series Beard administered glycine plus urea and found average increases in maximal work output per minute of 66 per cent in women and 79 per cent in men. In further studies the work rate was kept constant and the length of time it could be maintained was stated to be very substantially improved by glycine, glycine plus urea, creatine, creatinine and glycine plus urea plus phosphate. An increase of muscle power from glycine, as measured with strength tests, was reported by Chaikelis (80).

These favorable reports have been emphatically denied by a series of well-controlled experiments conducted by experienced investigators. Sixty grams of gelatin daily had no effect on women accustomed to experiments in hard work on the bicycle (189). Maison (263) utilized male subjects who had been trained for a year or more with the finger ergometer and found no effect on the muscles involved from either 15 grams of glycine or 60 grams of gelatin daily. Previous gelatin feeding is without effect on the work capacity of the gastrocnemius of the rat (231). Karpovich and Pestrecov (221) could find no benefit from gelatin in a variety of muscular work tests on young men. King and his colleagues (229) carried out elaborately controlled studies on 33 healthy young w ite men and negroes in athletic training and found that 4.5 to 6.0 grams of glycine daily for 3 weeks had no effect on work capacity though both glycine and placebos increased work performance by suggestion.

Interest attaches to studies in which objective measurements were made during performance of standard tasks on the treadmill where training effects are less prominent. Horvath, Dill and Knehr (204) found no benefit from glycine or gelatin in work output, work efficiency, oxygen supply in work, or the level of blood lactate attained. Similar results were obtained from athletes in supervised training (339).

It is difficult to reconcile the two sets of opposing reports. The negative reports are generally much more satisfactory in all technical aspects. At the present time the only conclusion possible is that if an effect of glycine exists it must be temperamental in its appearance. It is significant that Wilder, who was originally favorable, reversed his stand after further observations and concluded he could find no basis for belief in a beneficial effect of glycine in normal persons (397).

Alcohol. Alcoholic beverages supply a small but appreciable proportion of the total caloric intake to many men engaged in hard work (14). There are two major questions: 1) To what extent may alcohol provide energy for physical work? and 2) How does alcohol ingestion influence work performance?

The abundant early literature on alcohol metabolism was reviewed by Rosenmann (341). The combustion of alcohol in rest proceeds at a fairly constant but low rate and almost all alcohol ingested is metabolized. Alcohol ingestion produces little or no increase in basal metabolism (408) (165) (273). There is some parallelism between the extent of carbohydrate metabolism and the rate of alcohol oxidation in the body (70) (165) (117) and at least some of this oxidation takes place in the liver (285) (305). Ethyl alcohol is certainly capable of utilization for some physiological purposes such as are involved in growth (283). Whether it can serve as a fuel for muscular work is another question. It is probable that muscles cannot utilize alcohol directly (254) (282), but this does not exclude an indirect contribution to the economy of exercise. The conclusion that alcohol may be used in work has been drawn by various workers (10) (165) (271) (359) and denied by others (67) (72) (309). The evidence offered is chiefly from respiratory quotients in rest and in exercise after alcohol. The R.Q. for complete combustion of alcohol is 0.67 and, since the quantities of alcohol involved are small, it would be technically difficult to establish the point. If it is considered that oxidation may be incomplete then none of the evidence is pertinent.

It has long been known that alcohol reduces the appreciation of fatigue so that the total voluntary work output of muscles may be increased although their capacity for contraction is decreased or unaffected (144) (250). Alcohol taken immediately before work may have an initial facilitation affect but the work output is reduced 30 minutes or so after ingestion (188). When large amounts of alcohol (240 cc.) are ingested by an habitual drunkard the output of heavy manual work is unchanged or slightly increased up to 4 hours later but a marked reduction is found after 12 hours

(14) (273). When the work involves a certain amount of skill and coordination alcohol always causes a reduction in work accomplishment (163) (372) (373).

Miscellaneous substances. At one time or another a great number of special substances in addition to those already discussed have been claimed to increase work capacity and to reduce fatigue. Some of these can or do enter into the total dietary in some cases and accordingly might merit brief mention here. Bøje (41) has reviewed the field in a brief critical discussion of "dopes".

Caffeine, as supplied in tea and coffee, is widely believed to reduce the appreciation of fatigue and there are reports that more direct effects on the muscles may be involved (338) (345). Results with hard work on the bicycle ergometer indicate a real benefit of caffeine-containing beverages on endurance (345). Foltz, Ivy and Barborka (145) showed a beneficial effect on recovery from fatigue in 2 subjects with 0.5 gm. of caffeine injected intravenously, but even larger doses were needed with 2 other men. In brief (anerobic) work both negative (195) and positive (230) results are reported.

Materials derived from the cola nut are widely used in beverages and, especially in northern Europe, in chocolate confections (e.g., "Scho-ka-kola"). The effects resemble those of caffeine (3). The results of rather extensive controlled studies clearly indicate an effect on willingness to continue in hard work (164). Whether there are effects peripheral to the central nervous system is not known. Cola preparations, like coffee and tea, tend to increase practical work output when used in moderate amounts at proper times in practical situations.

Atzler and Lehman (12) have claimed that lecithin in dosages of 22 to 83 grams per day has a beneficial effect on muscular performance. The interpretation of the test used is open to question and the data scarcely warrant the conclusions drawn by the authors in favor of foods containing lecithin. It should be noted that there is no evidence that lecithin is absorbed as such from the gut; certainly most of it is destroyed there.

Space here does not permit a discussion of substances like coca leaves and betel nuts which are chewed but not eaten. Their effects on work output may be appreciable but they should properly be considered as pharmacological agents rather than foods.

Military rations. The epitome of practicality in food for physical performance should be reached in military rations. Actually none of the present military forces of the world has attacked the problem with sufficient vigor and technical knowledge. The first requisite is the proper definition of tactical requirements; its absence has been a limiting factor which hinders efforts to develop the best rations for different operations. A second difficulty has been the necessity, or belief in such necessity, of making all rations conform to the high standards of the National Research Council recommendations for general subsistence. It can be argued that these recommendations for continued subsistence need have little relation to the food provided for operations lasting from a few days to a few weeks. Actually, U. S. Army rations provided for such operations—Rations C and K, and B ("5 in 1")—represent a compromise.

It should have been clear from the discussion so far that for limited periods of time vitamins, minerals and dietary balance may be of small consequence. If caloric needs are not too far from being satisfied and if the balance of fats, proteins and carbohydrates is not too abruptly and drastically altered, we may consider the major problem of combat rations fairly well solved. Of course this assumes that the rations offered are sufficiently palatable and varied to ensure their consumption.

An important characteristic of military operations is the frequency of occasions when ration supply may break down and the troops must subsist on half rations or do without food for some days or even longer. The rations provided for and prior to such operations should take cognizance of this special nutritional situation. Generally speaking, it seems that military rations should be specialized for maintenance, for operations and for preparation for operations involving hazards to the ration supply. Specialization of the rations for different regions is much less important. There is no evidence that the nutritional needs in deserts, wet tropics and the arctic are essentially different. Adjustment of the physical properties of the foods and convenience in their preparation under various circumstances requires study but is outside the scope of the present discussion (210) (226).

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Symposium: Can the Euphoric, Analgetic and Physical Dependence Effects of Drugs Be Separated?

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The papers presented in this Symposium constitute independent views of four authors concerning the question "Can The Euphoric, Analgetic, and Physical Dependence Effects of Drugs be Separated?" It is well known that the opiates, and possibly Demerol, are the only analgetic drugs which are capable of producing all three phenomena. Certain drugs may produce analgesia and/or euphoria in man without causing physical dependence. The ideal analgetic would be a drug having minimum euphoric and physical dependence effects. It can be argued that the euphoria factor of opiates plays a distinct rôle in the relief of pain; the pain still being discernible, but the sensation is masked by a dominant sensation of euphoria or well being. Others claim that analgesia is a distinct property of analgetic drugs and is independent of the euphoric factor. In certain people not having pain there is a feeling of euphoria following morphine, while in the same individual or others having pain morphine produces only relief of pain with little or no apparent euphoria. Morphine dysphoria is also noted in some normal people not having pain. When an individual takes repeated doses of an opiate, there is developed a third phenomenon called physical dependence, which is an undesirable side action. Despite this factor no drug is known to be as effective as morphine for the relief of pain. When the chemical structure of morphine is altered to

decrease its addiction liability, there is generally a corresponding decrease in its analgetic properties. This then raises the question as to how intimately are euphoria and physical dependence associated with a drug to make it an excellent analgetic comparable in effectiveness with morphine, and how can dissociation be effected? The subject matter of this symposium is not limited to the opiates, but includes some of the non-opiate analgetics as is discussed in Part III.

The discussion of this problem was proposed for a dinner meeting of the Drug Addiction Group to be held in connection with the Federation of American Societies for Experimental Biology at Cleveland in the Spring of 1943. Four speakers were invited to discuss key aspects of this problem. Due to the war emergency and restrictions in travel, the Federation meetings have been postponed. In order that progress in this field not be interrupted too severely, the guest speakers have agreed to prepare their talks in the form of a published Symposium. The views presented by each speaker are independent, and in some instances, may be in opposition with each other. It is hoped that various ideas presented will serve to stimulate thought, to raise further questions, and to give opportunity for exchange of ideas for further research on new analgetics and on problems of drug addiction. It is planned that when the Federation meetings are resumed, that this subject will be the topic for an after dinner meeting.

I. WITH REFERENCE TO EUPHORIA

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Euphoria is defined as a feeling of well-being and buoyance, an indication of good health. Its antonym is dysphoria, a feeling of ill-health and discomfort.

This word has, in medical circles, acquired a meaning quite alien to its proper one. It is used rather regularly with reference to the emotional state of the paretic and as a term of reproach to drug addicts suggesting that the addict is trying to obtain a feeling of well-being, buoyance and good health to which he is not entitled. The implication is that the addict should be satisfied with discomfort and unhappiness and that the search for euphoria on his part is wrong.

The explanation of this distortion of a word otherwise without moral connotation seems to be that there are probably two kinds of euphoria which might, for convenience, be designated as true and false. True euphoria is present either when the body is in the highest degree of health with abundant energy and a well established and stable homeostasis, or when the cause of some discomfort or pain is rather suddenly eliminated. False euphoria occurs when a discomfort or pain is masked by medication which creates insensibility or indifference to a still existing situation.

The condition to be relieved or masked before euphoria occurs may be either in the external or in the internal environment. As an example of an external environmental situation the relief of which causes euphoria, we may consider the effect on the individual of a state of war. Tension, worry, uncertainty, associated with the war, produce in many persons a rather high degree of dysphoria. If, as occurred on November 11, 1918, it appears that the cause of this unhappiness has been dissipated, a very marked euphoria occurs resulting in such demonstrations as the Armistice celebration at that time. This could be considered as an example of true euphoria. If on the other hand, an individual, without waiting for the war to terminate, uses alcohol or drugs to dull his realization of the situation, the resulting euphoria would be the type which has been designated as false.

For an example of internal environmental abnormality producing dysphoria, we may take an attack of paroxysmal tachycardia. During the attack definite dysphoria exists, and when the attack ceases a positive euphoria is usually experienced. If while the attack continues the person seeks relief by the use of an opiate or some other drug, for example alcohol, the euphoria which might result could be designated as false.

The chronic euphoria which exists in the hypomanic and the spectacular changes in mood occurring in the cyclo-thymic personality may possibly be related to changes in the vegetative nervous system. Improvement in research techniques, especially along the line of chemistry, biology and physics, must be made available before this problem can be approached. The classical picture which sometimes occurs as a symptom of dementia paralytica can probably be related to lesions in the higher centers of the nervous system. It is suggested that these lesions

produce an effect analogous to that produced by pharmacological action in lessening the activity of higher centers. The resulting euphoria may be regarded as a false one on a relatively irreversible organic basis.

The production of a false euphoria by medical treatment must not be regarded as improper or unethical. The practice of medicine, especially of surgery, would be almost entirely impossible if it were not for our ability to produce during the post-operative state a false euphoria by the proper administration of opiates or other drugs. It is the desire of people for euphoria which has created the medical profession. Patients are not interested in fine-drawn philosophical distinctions as to whether the sense of well-being is due to the relief of the condition or to the masking of it. What they seek is the relief of dysphoria and the production of euphoria. It is, of course, the responsibility of ethical physicians to restrict the production of false euphoria to absolutely necessary situations, but no hesitancy must be exhibited in producing this false euphoria, especially in the treatment of such conditions as shock.

The abnormality of the internal environment which is designated by the term "tension" is an important factor in the occurrence of dysphoria, and its relief is usually associated with euphoria. Many mental states, most of them unpleasant but some of them pleasant, produce more or less profound disturbances of the vegetative nervous system. Whether a line can be drawn between the ideational concept of an emotion and its physiological accompaniments is probably a philosophical hair-splitting which is unproductive and which represents a tendency toward metaphysics. The facts are that a high degree of emotional disturbance is associated with such unpleasant and uncomfortable physiological disturbances as irregular heart action, headache, pylorospasm, hyperactivity of the gastro-intestinal tract, flushing or peripheral vascular constriction, and the like.

Unfortunately, we do not have objective methods for studying and measuring tension. A beginning is being made, but a much more refined approach to the problem is necessary. When this is developed, our understanding of personality, the use and misuse of drugs and the change of dysphoria into euphoria will probably be much simplified.

There are probably three aspects to this dysphoria, namely, tension, disturbance in homeostasis, and what may be termed physiological unhappiness. These cannot be separated and in fact may be identical, merely different ways of looking at the same phenomenon. It is recognized that a high degree of discomfort associated with these three aspects occurs both with neurotics and with psychopathic individuals and is one of the principal sources of their discomfort. Its relief may lead to an immediate reversal of the person's attitude toward himself and toward his external environment.

It is interesting to speculate as to whether relief of tension might be considered a false or true euphoria. In other words, is the relaxation of muscle spasm or the relief of an irregular heart action an elimination of the source of the discomfort, or is this merely a temporary masking of symptoms? The answer to this question depends very largely upon the mental attitude of the worker. It is possible that when the peripheral manifestations of an emotion can be safely and properly relieved it will be found that the unpleasantness of the emotional state will have been dissipated. If this conjecture is true, we may find that true euphoria can be produced by action on these terminals without any necessity to obtund the higher centers.

Analgesia refers to the relief of pain. It is, of course, difficult to draw the line between a severe discomfort and a mild pain. This rests very largely upon the individual's interpretation of his sensations. For example, some persons have, traditionally, a stoical attitude toward discomfort and pain and minimize suffering of any sort. Others have a very low threshold for either physical or mental pain. Neurotic and psychopathic individuals frequently exhibit very low thresholds for pain and for discomfort. Much of the trouble which the psychopathic individual engenders is closely associated with his complete inability and unwillingness to endure any discomfort, whether this be in the sociological, psychological or physiological fields. The problem is further complicated by the fact that pain produces tension which in turn produces more pain, thus creating a vicious cycle. When this cycle is broken at any point, either by an analgetic or by a substance which dissipates tension, euphoria is very commonly experienced. Whether this is a false or a true euphoria need not trouble us if the method of relieving either the pain or the tension is one which does not have dangerous repercussions either in the physiological or the sociological fields.

Physical dependence has been demonstrated only for opium and its derivatives and for demerol. Since the work on the latter drug is fairly recent and has not as yet been confirmed by other workers, it will be well to confine this discussion to the relationship of euphoria to the physical dependence which develops following prolonged use of opiates.

When a presumably normal individual is given an injection of morphine, dysphoria rather frequently results. This may vary in degree from a

mild feeling of anxiety to fear, nausea, and vomiting. When a normal person suffering from a severe pain receives enough morphine to relieve his pain, euphoria usually occurs without these manifestations. When a former addict receives a dose of morphine, euphoria rather regularly occurs. Sometimes with presumably normal, pain-free individuals, euphoria instead of dysphoria will follow an injection of morphine. Investigation of this small group should be carried out to determine what the types of the personality are and whether these might be considered as potential narcotic drug addicts.

The repeated administration of opiates rather rapidly results in the development of tolerance. As this occurs the addict develops physical dependence, and his struggle is to obtain sufficient drugs to prevent the dysphoria associated with the withdrawal syndrome. However,. he still strives, by increasing his dose, to attain his earlier experience of euphoria. By this increase in dosage he increases both tolerance and physical dependence, thereby establishing a vicious cycle which is probably responsible for many of the legal and social difficulties in which narcotic addicts become involved.

Other drugs also exhibit a marked variation in their results. For example, with certain persons the ingestion of a moderate amount of alcohol produces euphoria, while excessive doses destroy it, causing either depression or an attitude of hostility and aggressive anti-social activity. With other persons, no overdose will take away the feeling of euphoria. With others, again, euphoria never occurs, the initial effect of the drug being at once to relieve depression or hostility. The same individual at different times may show deviation from his usual response. For example, the period of euphoria may be brief or may not appear. Possibly this can be related to conditions of absorption and excretion, and specifically to the concentration of alcohol in the brain. If it were possible to determine at frequent intervals the alcohol content of the brain, we might find that there is a definite relationship between a particular mental state and the concentration of alcohol in the nervous system.

With barbiturates, the route of administration has an important relationship to the production of euphoria. Almost invariably, irrespective of the type of personality or the state of internal environment, a small dose administered intravenously will produce a strikingly uniform euphoria, with affability, accessibility and a sense of well-being.

Certain persons exhibit very marked symptoms of intoxication associated with aggressive anti-social activity following the administration of barbiturates. In some persons of this type who have been studied, it has been found that an encephalopathy is present, and it is quite probable that this effect may be the result of brain damage, possibly resulting in decreased ability to utilize oxygen or an increased vulnerability to a decrease in the supply of oxygen.

The effect of benzedrine in changing an unpleasant mood to the opposite is interesting and puzzling. Most of the euphoria-producing drugs have the effect of relaxing smooth muscle spasm, of decreasing the activity of the sympathetic side of the vegetative nervous system. Benzedrine, however, has a sympathico-mimetic action, and yet with some people it produces a pronounced euphoria. Here is a fertile field for intensive study with improved techniques to unravel some of the riddles of homeostasis.

Very little is known about the euphoria-producing qualities of Indian hemp and its derivatives, the chief one used in this country being known as marihuana which is usually taken by smoking. Some persons attain a marked euphoria from it, and it is for this reason that it is used. It is reported that moderate over-dosage produces a state of fearfulness and uneasiness and that habitual users tend to limit their dosage much more definitely than do the users of opiates. Work is now being done with a standardized preparation of the active principle, and it is hoped that some definite information can be obtained. It is possible that suggestion and group psychology play a considerable part in the production of the alleged effects of this drug.

Demerol in some persons produces a definite euphoria in the absence of pain. It may be that these are persons who are suffering from an undue amount of tension resulting in smooth-muscle spasm and that euphoria is the result of the release of this spasm. Until we have an objective quantification of tension, here, as with other drugs, our conclusions must be empirical and tentative.

Conclusion. It is suggested that the explanation of the disrepute into which the word "euphoria" has fallen is that there are probably two kinds: true, when an abnormal situation is dissipated, and false, when the situation is masked by obtunding some part of the nervous system.

Euphoria can in some instances be related very definitely to analgesia since relief from pain will usually produce it. However, in many other cases, euphoria arises from relief of discomfort, worry, tension, physiological unhappiness or depression.

Euphoria from the use of opiates tends to be less easily attainable with the development of physical dependence, and in this sense these phenomena may be considered as antipathetic to each other; the higher the degree of physical dependence, the less easily is euphoria attainable, and the less the physical dependence, the more easily does euphoria occur.

The search for euphoria is sound biologically. Our goal should be the attainment of a true euphoria by the elimination of the situation which causes dysphoria. However, it is frequently necessary to resort to what has been tentatively designated as false euphoria, sometimes in order to save a life, sometimes only to make life reasonably tolerable. The methods by which people seek euphoria are sometimes harmful or dangerous, but the desire to attain a feeling of well being and buoyance is not to be condemned.

When we have a better knowledge of human physiology and of its control, we may be able to obtain for our patients, including actual and potential drug addicts, a true euphoria. When this knowledge and control have been obtained, the prevention and cure of narcotic drug addiction may be greatly simplified.

II. WITH RELATION TO ANALGESIA AND CLINICAL EXPERIENCE

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Webster's New International Dictionary of the English Language (Merriam Co., 1932) and Dorland's American Illustrated Medical Dictionary in its nineteenth edition agree that euphoria indicates a "bearing well," the condition of feeling well, a sense of good health and bodily comfort, an absence of pain or distress. There has been a tendency among those who work with opiates to depart from this strict definition. The euphoria produced by narcotics is interpreted by these workers as something more than the normal sense of physical and mental well being. Their inclination is to attribute to the drugs an ability to cause exaltation or an abnormally pleasant lassitude. This broader interpretation will be used for euphoria throughout this paper.

Seevers (1) indicates that pain may be relieved by 1, abolition of pain stimuli; 2, blockade of pain pathways; 3, increase in pain threshold; 4, modified pain reaction pattern; 5, induction of sleep, stupefaction or anesthesia. Any one, or all of these can be called analgesia, which leads to the definition of analgesia as an absence of pain, whether in health or disease. There can be little doubt in the mind of anyone who has really considered the matter that euphoria in the sense of an abnormal stimulation or depression of mind is not necessarily associated with analgesia. Proof of this, if any is needed, lies in the fact that the principles listed by Seevers can be introduced in many different ways and under quite different conditions. Methods of introducing these principles include psychic, surgical, roentgoenological, possibly endocrine, and even pathological. This is illustrated by the examples of the psychologically induced increase in the pain threshold and modified reaction to pain during the excitement of an athletic contest or sexual intercourse; in the surgically induced blocking of pain pathways following successful rhizotomy or cordotomy for whatever cause; in the radiologically induced abolition of pain stimuli afforded patients given deep x-ray therapy to relieve pain from osseous metastases of various carcinomas; in the analgesia, apparently endocrine induced, afforded sufferers of pain from metastatic carcinoma of the prostate who have undergone orchiectomy or stilbesterol treatment (2); and in that pathologically induced interruption of pain pathways resulting from the bizarre affliction syringomyelia. It becomes necessary, then, to establish a further definition of terms before continuing the discussion. The title question must be restated to ask, "Can a drug-induced absence of pain be distinguished from a drug-induced sense of abnormal well being and bodily comfort; is physical dependence at least in part a factor of this euphoria; and is it possible to preserve the drug induced analgesia while eliminating the drug induced euphoria and physical dependence?" On this basis concern may be limited to whether or not one can separate three drug effects in an individual susceptible to drugs capable of producing these results. Automatically we are reduced to a consideration of the opium derivatives, Demerol, and possibly cocaine and alcohol, since these are the only drugs recognized as capable of producing a degree of analgesia, euphoria and physical dependence. The position is further simplified since cocaine is now of so little importance as a drug of addiction, alcohol is seldom considered a drug of addiction, and Demerol is so little known and available only for experimental purposes.

In their work with morphine and its derivatives both the pharmacologist and the clinician attribute to these drugs the ability to cause, to a greater or less degree, certain specific actions in human and animal subjects. Furthermore these actions are thought to be related directly to the chemical structure of the drugs and to be alterable with variations in the molecule. Himmelsbach (3) has investigated the effect of chemical variations of

the phenanthrene group on the potency and duration of physical dependence action of each of ten related drugs of the morphine, codeine series. Eddy (4) has studied toxicity, convulsant action, general depressant, analgesic, exciting, emetic and respiratory effects in various animals, and he adds that, "The administration of morphine to man, at least in many individuals, not only relieves the discomfort of pain and restlessness but also causes a pleasurable feeling of well being, a 'euphoria'." The suggestion is that this "pleasurable feeling" is in itself an entity, the direct result of opiate action. Such recognition further supposes that "euphoria," being a separate entity, is variable independent of other morphine effects when the basic molecular structure of the drug is altered. This asks no more of euphoria than of the other recognized effects of morphine that can be increased or suppressed by small alterations in the molecule. An example with which all are familiar is the decreased stimulating and depressant action obtained in the simple change from morphine to codeine. Dilaudid and Metopon show changes to lesser degree with a definite increase in analgesic action and decrease in hypnotic effects. The premise is further substantiated by the addict who prefers heroin's subtle seduction, accepts the grosser joys of morphine administration, and disdains the impotent codeine. In the administration of morphine and related drugs we must, therefore, agree with Doctor Eddy's implication and isolate from the ability to allay pain, i.e., analgesia, the stimulating or depressant action, i.e., euphoria, created by these substances. It is necessary at this point to insist that in those persons who are in a normal state of psychological equilibrium in relation to the immediate environment and circumstances morphine administration is not always a pleasant experience (5).

In considering the relationship of analgesia and euphoria one must recognize the concept that analgesia from drugs moves only from severe pain to less severe pain. That is to say that analgesia has only a unidirectional effect. Euphoria, on the other hand, is bidirectional in its effect since it can be the result of stimulation from a phase of hebetude, or depression from a phase of agitation. It is in the persons abnormally depressed or excited that morphine tends to produce euphoria. The drug effects move them away from their abnormal, and therefore probably objectionable, psychic state toward, or in some cases through normalcy. The rate at which this change is made and the amplitude of the swing to or from normal determines in great degree the intensity of pleasant or unpleasant effects of the drugs. In addition the comfort or discomfort induced by the drug is altered by the intensity of the side effects accruing from drug administration. When we speak here of an abnormal psychic state it is not necessary to consider the patient a candidate for psychiatric consultation. Normality and abnormality are entirely relative to the existing psychic state of the individual in his relation to the immediate environment and circumstances. This is repeatedly demonstrated in following preoperative cases before anesthesia is started, and is particularly prominent when the preoperative narcotics are given intravenously. Obviously this is the method by which the most rapid alteration in psychic state is produced and serves to emphasize again the importance of the rate of change. In a patient in normal psychic equilibrium in relation to the existing circumstances stimulation or depression would be a move toward the abnormal, and as such it would probably be interpreted as unpleasant. This point of unidirectional analgesia and bidirectional euphoria is outstanding in importance since it is one where the characteristics of analgesia and euphoria do not overlap.

Euphoria is to be considered one of the undesirable side actions of morphine when the effect desired is analgesia alone. As such it can be included with the toxic, convulsant, emetic, respiratory depressant, and dependence producing actions of the drug. We recognize that members of the feline family, pigs, horses, goats and some women gain from morphine administration an excitatory stimulus which, with sufficiently large doses of the drug, progresses to absolute mania. It is impossible in the present stage of our knowledge to exclude the possibility that the drug-induced state of euphoria is this same excitatory response altered only in degree. Also the depressant effects of the drug may well be interpreted as euphoria in the patient brought from a stage of great agitation to one of pleasant lassitude. Recognition must be given to the probability that early habituation to the drugs and later dependence upon them is, at least in part, a factor of this euphoria. Certainly it is usually the main object which leads the inebriate individual to seek repetition of the experience in the early stages of addiction. Lawrence Kolb (6) condones this thinking when he says that a majority of addicts are persons of inferior psychic makeup striving by means of the drugs to more nearly approach normality; and he justifies their attempt when he claims that many addicts supplied with adequate amounts of drug are better and more useful citizens than when they are kept abstinent. Let me emphasize that he is speaking of inebriate individuals, not the psychologically normal patients who have been accidentally or necessarily brought to physical dependence during the therapeutic use of the drugs.

There is a definite variation in the intensity of

the stimulating action of morphine depending upon the mode or route of administration. The intravenous route has been shown to be that from which the greatest stimulation is obtained (7). Addicts who use the intravenous method prefer it mainly because of the speed with which drug effects are obtained and the gratifying initial jolt which occurs when the drug is injected. In both the intravenous and the subcutaneous methods of taking the drugs the needle's peculiar association with addiction is a consideration. Euphoria, as well as all of the other effects, is far less marked with oral and rectal use of the opiates. This is probably due to the slower absorption and consequent lower total dose in the circulatory and central nervous systems at a given time.

The question of duration of euphoria is difficult to settle in the present state of our knowledge. In considering the action of the morphine derivatives it can be generally stated that an increased speed and intensity of analgesic action is accompanied by increased addiction liability of the drug and a decreased duration of action. In the absence of any objective data on this point we can only suggest that this is probably also true of the euphoria inspired by these substances.

The size of the narcotic dose should be considered in any discussion of the euphoria initiated by the opiates. Wolff, Hardy and Goodell (8) claim that therapeutically these drugs are mainly dependent upon a) pain threshold raising action; b) dissociation of pain perception from the usual reaction to pain; c) induction of lethargy and sleep. The pain threshold raising action and a degree of dissociation from pain reaction are the effects for which we should strive in using the drugs as analgesics. Complete dissociation from pain response and the induction of lethargy and sleep are, in the mind of this author, the result of morphine overdose and tend to the production of euphoria and physical dependence. In early use of the drug they are more prominent but differentiation is soon possible in cases using morphine longer than three or four days. This might be considered evidence of the speed with which tolerance can be developed to these effects. We fail to recognize in many instances that there is a limit to the analgesia we can expect from morphine, and many of us unfortunately attempt to overcome this limitation by the administration of larger doses given at shorter intervals. In so doing we invite emphasis upon the undesirable effects of the drugs. It is necessary to stress the belief that morphine should be used in its minimal effective clinical analgesic dose and that its effectiveness should be judged entirely on the basis of analgesia. If hypnosis is desirable in a specific case it can be obtained by the supplemental use of a barbiturate rather than increased morphine intake. This author is convinced that in a large majority of patients analgesia is obtained with doses less than are necessary to cause the undesirable euphoric effect.

In personal dealings with patients it has been a practice, in spite of the history and family insistance that the patient is in great need of large doses of narcotics, to completely withdraw these drugs from anyone referred for recommendations as to control of pain. This rule is modified if the patient is obviously in extremis or it is agreed with the referring physician that we are justified in the use of morphine for its psychological effects of freedom from anxiety, relaxation, contentment, apathy, depressed mental ability, and sleep. These effects are admittedly desirable in some cases, particularly those requiring only a few doses of narcotics to control acute pain accompanied by psychic trauma. Withdrawal in all others is instituted first to demonstrate the need for narcotics to control pain; second to determine, if abstinence can be maintained sufficiently long, whether or not previous narcotic experience has left the patient in any degree dependent upon the drugs; and third to afford a foundation of definite knowledge upon which to lay plans for the further use of narcotics in the control of the patient's future pain. Withdrawal is continued only long enough to afford the necessary information. The number of patients who, with good nursing care, are more comfortable when taking very small doses of narcotics or when completely abstinent from these drugs is a continual source of surprise. Maintained on these lower doses patients remain comfortable and avoid dependence far longer than when the drugs are given in larger doses and judged for effectiveness on the basis of hypnosis and psychic stimulation or depression. This can only be interpreted as further proof that opiates used in their minimal effective clinical analgesic dose do not produce mental pleasure in most individuals.

Analgesia and euphoria are both subjective phenomena. As such they are dependent upon the existing psychic state of the individual in relation to the immediate environment and circumstances. Since this is true both analgesia and euphoria can be defined in relative as well as absolute terms and values. Both analgesia and euphoria may be altered by the strength of the pain stimulus and either or both may be altered by the strength and character of the drugs employed. The speed of change from a relatively abnormal psychic state to one relatively more normal, and the amplitude of this change are largely the determining factors in the intensity of euphoria produced by a drug. Drug effects are further dependent upon the algebraic sum of pleasant and unpleasant results accruing from their use. We must admit that we

have not brought to the clinic an opiate which affords the desired analgesia without the tendency to cause physical dependence in the vast majority subjected to prolonged use, and euphoria in a small minority no matter what the duration of narcotic experience. Thus we are forced to the conclusion that these factors are apparently inherent in the pharmacologically active phenanthrenes, and that to avoid them we must turn our investigation to other chemicals for a drug affording analgesia alone.

SUMMARY. Euphoria, as interpreted by those who work with narcotics, implies a pleasant psychic state beyond that of physical and mental normal.

Euphoria is not necessarily associated with analgesia when analgesia is defined as an absence of pain, whether in health or disease.

Euphoria, analgesia and physical dependence are separate effects of morphine and its derivatives. As such they can be differentiated in the patient, and can be independently altered with variations in the morphine molecule.

Morphine effects are not a universally pleasant experience.

Euphoria is to be considered one of the undesirable side actions of morphine administration when the objective in the use of the drug is analgesia alone.

Euphoria may be the excitatory or the depressant response to morphine altered only in degree. The amplitude of the change toward psychic normality in relation to the immediate environment and circumstances, and the speed with which this change is effected determine the intensity of euphoria. This stimulation or depression is usually the object in the inebriate's attempt to repeat the experience of morphine administration in the early stages of addiction.

The mode of administration of morphine causes a variation in the intensity of the actions of the drug.

It is a general rule that addiction liability is greatest in those morphine derivatives with a rapid, intense and short lived analgesic action. It seems probable that euphoria follows this same general rule.

There is a limit to the analgesia we can expect from morphine. In attempting to overcome this limitation by the administration of larger doses given at more frequent intervals the patient is exposed to the unnecessary and undesirable side effects of the drugs.

Morphine should be administered in its minimal effective clinical analgesic dose and its effectiveness judged solely on the basis of analgesia unless the case is one of acute pain and accompanying psychic trauma where the psychic effects of the drug are desirable. When narcotics are administered in their minimal effective clinical analgesic dose patients remain comfortable, euphoria is largely avoided, and the development of dependence is considerably postponed.

If hypnosis is desirable in a specific case receiving narcotics for analgesia the addition of a barbiturate hypnotic to the morphine analgesic is a satisfactory procedure.

Analgesia from narcotics occurs with doses below the level required to cause euphoria.

Unless the patient is obviously a terminal case or we admit that we are using narcotics for their psychological effects complete withdrawal for a period when first evaluating the case allows: *a*, Proof of the patient's narcotic necessity; *b*, an estimate of the existence of dependence developed during previous narcotic experience and; *c*, affords a foundation of definite knowledge upon which to base decisions as to further use of narcotics for the control of future pain.

CONCLUSIONS. We have been unable to bring to the clinic an opiate which preserves the desired analgesic action, eliminates the development of physical dependence and which, in excessive doses, does not produce euphoria in a small group of patients.

The factors euphoria, analgesia and physical dependence are apparently inherent and inseparable in the pharmacologically active phenanthrene derivatives although their intensity can be altered independently with variations in the molecule and their presence differentiated in the patient.

It is steadfastly maintained that euphoria, analgesia and physical dependence can be separated. It seems probable that to produce a drug which affords analgesia alone one must turn to chemicals other than the phenanthrene group.

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III. THE NON-OPIATE ANALGESICS

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The original purpose of this communication which was to introduce this phase of the subject for discussion has been retained, and therefore, this review is intended to be neither complete nor conclusive. The drugs of this group will be briefly explored in the light of the question: "Can the euphoria, analgesia and physical dependence effects of drugs be separated?" Only those drugs which have some analgesic effect after absorption will be discussed. This excludes the local anesthetics such as cocaine, and other drugs which produce analgesia by local action.

The non-opiate analgesics include a large number of drugs of widely different chemical structure. The following have been chosen for discussion: Demerol, Alcohol, Acetanilid, Acetophenetidin, Antipyrine, Aminopyrine, Salicylates, Barbiturates, Trichlorethylene, Ergotamine, and Caffeine.

A number of reviews are available which consider various aspects of this subject: theories of drug addiction, pharmacology of drug addiction, and a consideration of euphoria, analgesia habituation, tolerance, physical dependence and withdrawal syndromes (1–4); demerol (5); alcohol (6, 7); synthetic analgesic-antipyretics (8); aromatic amino and nitro compounds (9); acetanilid (10); acetophenetidin (11); salicylates (12); barbiturates (13, 14); and therapeutic agents of the quinoline group (15).

Demerol, a new synthetic analgesic possessing certain properties similar to those of morphine and atropine, was introduced by Eisleb and Schaumann in 1939 (16). Demerol (1-methyl-4-phenylpiperidine-4-carbonic acid ethyl ester hydrochloride) has also been known as Dolantin, Eudolat, Dolantol, and D-140. Climenko (17) has suggested that the compound has a certain structural similarity to atropine and morphine.

Pharmacological studies have been carried out by a number of investigators (16–21). The acute toxicity is relatively low except on intravenous injection when the drug produces a fall in blood pressure apparently due to peripheral vasodilation (20). Chronic toxicity studies by Gruber et al. (20) on dogs revealed that 100 mgm. per kgm. per day produced hyperirritability, spastic extension of all extremeties, unsteady gait, mydriasis, rapid shallow respiration, and clonic convulsions precipitated by noise or touch; these symptoms subsided before the next dosage. In these and other experiments, no development of tolerance was observed to these effects. Climenko (17) obtained no evidence that experimental animals developed physical dependence; a slight sedative and a marked analgesic action on mice, rats, cats, dogs, and monkeys was observed. The effect of demerol on the gastrointestinal tract in animal experiments has been variable depending upon the animal used and the method of study (17–21; but see 5). However, a number of workers have reported a spasmolytic action on preparations of quiescent gut or that spastic to acetylcholine, histamine, and barium chloride (17–21). Nevertheless, Gruber et al. (20) found the response unpredictable in several different types of preparations. Climenko (17) states that the spasmolytic effect is due partly to an atropine-like action, and partly to a direct smooth muscle depressant action. As we shall see, most of the evidence indicates a spasmolytic action on smooth muscle in man. The sedative effect of the drug in animals is apparently weak (17, 19, 20). However, it has a potentiating effect on the hypnotic action of sodium evipal (22) and sodium pentothal (23). It decreases the induction time and prolongs the anesthetic time of nitrous oxide-oxygen (21), and decreases the amount of cyclopropane required to produce anesthesia (23). In man, cutaneous pain threshold studies (17, 21) (Wolff-Hardy technic, 24) showed that 100 mgm. orally produced a maximal elevation of the threshold of 50 per cent in one hour which returned to normal in 6 hours. With intramuscular injection, the peak was reached in 45 minutes; it was found that 50 mgm. was as potent as 22 mgm. of codeine, and that 125 mgm. produced as much elevation as 17 mgm. of morphine but was of shorter duration.

The chief clinical therapeutic effects are analgesia, spasmolysis, mild to moderate sedation; euphoria is observed in some cases. The practical

use of this analgesic effect in man has been applied to the relief of pain due to a large variety of conditions (see 5, 20, 23 for references and infra). Visceral pain such as that arising from the peritoneum, pleura, or smooth muscle is relieved more effectively than pain arising from skeletal and neurological structures (5, 25). Clinical comparison indicates that the parenteral administration of 100 mgm. of demerol are equivalent to 10 mgm. of morphine (5, 25). Satisfactory results have been reported for the use of the drug for pre-operative medication (23), post operative patients (5, 25; see 23) and for obstetrical analgesia (26–28 and others). Spasmolytic effects have been reported by Batterman on the gastrointestinal tract (5, 25), by Climenko and Berg (29) on the ureter, and by several observers (18, 20, 30 and others) on the bronchial musculature. The sedative effect is mild but apparently useful in a number of clinical conditions. Tolerance is developed to the sedative effect (5). With respect to clinical toxicity, nausea and vomiting occur in a small percentage of cases, some patients complain of dizziness, perspiration, lightheadedness and zerostomia; extreme weakness occurs rarely. No evidence of toxicity to the hematopoetic, genito-urinary, or cardiovascular systems have been reported (5, 25).

In pain free "normal" individuals, demerol may produce a significant euphoria which is variously described. Although the subjective effects are pleasant to some, they may be somewhat disagreeable to others (5, 25). The morphine-like actions of demerol naturally raises the question of addiction liability. Several clinical reports have suggested that demerol may be habit forming (31–34).

The establishment of some measure of physical dependence in morphine post addicts has been reported by Himmelsbach (35). When rather large doses repeated at frequent intervals were administered mild abstinence signs were noted after 1 and 2 months when the drug was withheld for 24 hours. After 11 weeks, abrupt withdrawal produced a characteristic abstinence syndrome which, however, was less severe than after morphine. In morphine addicts with established physical dependence, demerol was substituted for 10 days and then abruptly discontinued. Support of morphine physical dependence by demerol was incomplete; after demerol withdrawal the signs of abstinence were intensified for 2 days, but were less severe than after withdrawal of morphine or codeine. On the other hand, Batterman (5, 25) has not observed the development of physical dependence in the ordinary clinical use of the drug in patients who were not post addicts. However, it is quite possible that abuse of the drug may produce habituation and physical dependence in certain individuals, although the liability appears to be less than with morphine.

A discussion of tolerance must take into account several actions of the drug: sedation, analgesia and cerebral stimulation. Tolerance appears to develop rapidly to the sedative action (5). Andrews (36) has noted in post opiate addicts that tolerance is rapidly gained to the pain threshold raising effects (Wolff-Hardy) when large doses of demerol are allowed. Tolerance was evident in 2 weeks and reached a maximum in 8 weeks. In another study (37) under similar conditions on post-opiate addicts, the subjects chose dosages which resulted in exaggerated tremors, graduating into muscle twitches, and finally into gross jerking of the extremeties, hallucinations, increased sensitivity to sudden noise, and weakness in the extremeties (these are similar to effects described in animals by Gruber et al.). Electroencephalograms revealed the appearance of slow waves after only a few days of demerol administration which progressively became slower and increased in amplitude. The slow waves persisted for 48 hours after withdrawal. These clinical and electroencephalographic changes are in sharp contrast to those observed in addicts receiving large regular doses of morphine within their limits of tolerance (37). Thus the post-opiate addict will choose dosages of demerol which exceed his tolerance for the cerebral stimulant effects. The dosages employed in these studies are large compared with those used for clinical relief of pain. It is probable that amounts greater than 150 mgm. every 3 hours should not be given (5). Tolerance to the *clinical analgesic* effectiveness of the drug have not been evident so far (5).

Alcohol is one of the oldest analgesics. In recent measurements of cutaneous pain thresholds, Wolff, Hardy and Goodell (38) observed that a single dose of 30 cc. of alcohol produced a maximal elevation of 45 per cent; larger doses produced no greater elevation but prolonged the duration; and frequently repeated doses sustained the elevated threshold. The maximal effect of alcohol was not increased by the additional administration of acetylsalicylic acid although the slower action of the latter appeared to prolong the effect. Induced pain did not appreciably alter the threshold raising influence of alcohol. However, alcohol produced a considerable elevation of the "alarm" reaction threshold. Subjective reactions included euphoria, relaxation, and freedom from anxiety of pain.

The psychological effects of alcohol are too well known to require comment. Most investigators agree that these are manifestations of central nervous system depression. The fundamental reaction is to make "reality less real," which may be interpreted as euphoria. It must be admitted, however, that the intensity and manifestations of

this reaction differ widely with the individual and the circumstances.

Various factors in the development of dependence on the effects of alcohol are extensively discussed by Bowman and Jellinek (6). They consider that "primary addiction" may develop almost immediately and is characterized by an intense psychic dependence to the extent that the individual has a craving for the effects of alcohol and is unable to break with the habit. This dependence is psychologically motivated and intoxication serves the purpose of creating an artificial adjustment to reality. A physiological basis for this type of addiction has not been established. It is of interest to note, however, that Richter (39) has observed rats to prefer solutions of 1 to 6 per cent alcohol to water, but apparently disliked higher concentrations. The taste threshold of 240 human subjects tested revealed a similar preference for alcohol, but in many instances they liked higher concentrations.

Further, in primary addiction Bowman and Jellinek (6) consider that both chronic alcoholism (i.e., objective mental and physiological effects resulting from alcohol) and evidence of physical dependence may be absent. However, "secondary addiction," which is the most common, develops as a result of prolonged and excessive drinking. The initial motivation may be to counteract the physiological effects of a previous bout, but eventually there is development of some degree of physical dependence and there may be evidence of chronic alcoholism. The resultant psychological pattern of this individual becomes indistinguishable from that of the primary addict.

The significance of physical dependence as used above is not clearly defined, although it is indicated as the criterion for secondary addiction. The withdrawal syndrome in the alcohol addict usually consists largely of psychological manifestations, although there is frequently evident sufficient increased irritability to require sedation. For the most part the physiological basis for alcohol addiction has not emerged beyond the stage of theories, of which there are quite a number (see 6 for references and discussion). Disturbances which have been observed in electrolyte and water balance (40, 41) may play a significant role. Pertinent to this point, too, are the observations of Davis et al. (42) on the influence of alcohol on the electroencephalogram in which slow waves appeared and tended to persist for some hours. Further is the well recognized relation of alcohol to seizures in epileptic patients. Lennox (43) has recently stated "apparently in man (alcohol) precipitates convulsive attacks only in those who are subject to seizures." Lennox points out, however, that this statement might be questioned with respect to persons who have convulsions only following intoxication and during the sobering-up process, and states that it would be important to know whether such individuals had pathology of the brain (from alcohol or other causes) or whether they had cortical dysrhythmia before the symptoms of alcoholism and seizures began. Kalinowsky (44) has recently presented an interesting discussion of 2 more such cases. The evidence is predominantly against the conception that alcohol withdrawal bears a direct etiological relation to delirium tremens, although the possibility that it may be one of the factors cannot yet be completely discarded. Recognition of the role of vitamin deficiencies associated with chronic alcoholism has thrown a new light on the physiological and neuropathic manifestations of this condition (6).

There is general agreement that a certain degree of tolerance develops to the effects of alcohol, and probably plays an important role in the development of chronic alcoholism. Bowman and Jellinek (6) believe that a distinction should be made between psychological and physiological tolerance. Bogen (49) reviewed the various mechanisms which have been suggested such as absorption, excretion, oxidation, etc. and concluded that none of them were adequate to explain the phenomenon. The recent experimental work of Newman and Lehman (45) and Newman (46) on dogs indicate that the mechanism is primarily an acquired tissue tolerance which increases with habituation and decreases with abstenence. Mirskey's (47) observations on humans suggest a very rapid adaptation of the central nervous system to a given concentration of alcohol. The evidence is insufficient to support the idea of an acceleration of the rate of oxidation of alcohol. As to the oxidation of alcohol, work from this laboratory (48) supports the view that the liver is the site of the initial oxidation and requires insulin for this purpose, and that insulin or insulin and glucose accelerates oxidation.

The *analgesic-antipyretic* drugs included in this discussion are the aniline derivatives, *acetanilid* and *acetophenetidin*; the pyrazolon derivatives, *antipyrine* and *aminopyrine;* and the *salicylates*. In relation to the factors being considered these drugs occupy a somewhat controversial position and the literature is too extensive to review in detail. They all possess some degree of analgesic action for certain types of pain arising from neural and integumental structures; they are usually ineffective for visceral pain. Individual differences are noted in their other central nervous system actions; it is questionable whether these effects in any measure constitute a true euphoria. There is no unequivocal proof that chronic use produces physical dependence. Habituation or psychic dependence on the analgesic action has

been indicated in a number of clinical reports. Invariably the primary motivation for continued use of these drugs has been for relief of pain, most frequently headache. Chronic intoxication is sometimes associated with effects on other physiological systems in addition to the central nervous system, e.g., blood. What relation, if any, these factors have to habituation is not clear, but they have been mentioned, especially in connection with acetanilid and acetophenetidin, as a secondary motivation for continuation of medication (see 10 for reference and discussion).

These drugs are often taken in various combinations, and also with other drugs, for example codeine, barbiturates, and bromides. Clinical reports often do not attempt to differentiate the effects of the individual agents. Relatively few quantitative *experimental* studies on man are available.

Many attempts have been made to quantitate in man the analgesic action of this group of drugs. However, so far the only successful study is that of Wolff, Hardy and Goodell (50). In general they found that the threshold raising effects following oral administration of 0.3 gram doses of acetylsalicylic acid, acetanilid, acetophenetidin, and aminopyrine were approximately the same. The maximal elevation of the pain threshold was approximately 30 to 35 per cent which occurred between one to two hours and returned to normal within three to four hours. Acetylsalicylic acid was studied in considerable detail. A progressively greater elevation of the pain threshold was observed on increasing the dose from 0.03 to 0.30 gram, but larger doses, including 1.80 gram only prolonged the effect. Repeated administration of 0.3 gram at two hour intervals resulted in a sustained elevation of the pain threshold. The effect of induced pain on the threshold raising action of acetylsalicylic acid and acetanilid was much less than occurs with the opiates. The combination of acetylsalicylic acid by mouth with codeine phosphate hypodermically produced no greater elevation of the pain threshold than each drug separately. Likewise the combination of 0.3 gram each of acetylsalicylic acid, acetophenetidin, and acetanilid produced no greater maximal elevation of the pain threshold than was observed with the individual drugs, although the duration of the analgesia was prolonged. Further, the combination of acetylsalicylic acid or acetanilid with a barbiturate resulted in no additive effect. No threshold raising action with 0.3 gram of quinine sulfate was observed. Antipyrine, salicylic acid and cinchophen were not tested.

In relation to subjective effects Wolff, Hardy and Goodell (50) have reported that in pain free subjects amounts of acetylsalicylic acid up to 1.8 grams produced only mild relaxation and lethargy. There was little or no effect on anxiety or tension except that restlessness was reduced, and there was no feeling of contentment, euphoria or apathy. However, with 0.3 gram doses of acetanilid some relaxation, drowsiness and difficulty in mentation were noted and concentration and attention were slightly impaired. Although restlessness was allayed and anxiety diminished there was no euphoria. The psychological reactions to 0.3 gram of acetophenetidin were similar to those produced by acetanilid. Aminopyrine in 0.3 gram amounts produced no psychological effects, except very slight relaxation. The authors point out that the psychological effects of acetanilid and acetophenetidin may add to the popularity and therapeutic effectiveness of these agents. The combination of codeine or a barbiturate with acetylsalicylic acid produced psychological effects characteristic of codeine or the barbiturate. There was an impression that the sedative actions of these cobinations were additive, although their effects on pain threshold were not. From the standpoint of clinical analgesia, such combinations are probably valid since it is now recognized that not only analgesia per se but also sedation and an altered reactivity to pain are equally important components.

The pharmacological basis for the subjective feeling of well-being which some individuals claim to experience after taking these analgesic drugs is not clear. Often it appears to result largely from relief of pain, but also may be due, in part to an altered reaction to pain, or possibly to other drugs present in a particular preparation.

The development of some degree of tolerance to this group of drugs is indicated by numerous clinical reports in which patients took progressively larger doses, usually for relief of pain. Very little was found in the literature concerning the mechanism of tolerance. In this connection acetanilid and acetophenetidin have been most frequently mentioned. Payne (51) observed tolerance to the depressant effects of acetanilid in dogs. P. K. Smith (52, 53), working with monkeys, and Stanton and Agricola (54), working with rats, observed the development of some tolerance to the depressant effects of acetanilid, but Smith did not observe tolerance to the analgesic action in monkeys. No quantitative observations on development of tolerance to analgesic effects in man were found, although clinical data have been so interpreted (10, 55, 56). Further studies on man are desirable, since development of significant tolerance would favor use of progressively larger doses leading to manifestations of clinical toxicity.

In relation to habituation or psychic dependence, acetanilid and acetophenetidin have been most frequently mentioned, salicylates rarely, and antipyrine and aminopyrine almost entirely on the

basis of their analgesic action in persistent pain. Almost all of the evidence in favor of this view comes from clinical reports. In the majority of these cases the drugs were taken for pain which persisted or recurred after discontinuation of the drug. Several reports, however, have emphasized the observation that while acetanilid and acetophenetidin were being taken for relief of headache, the headache disappeared on discontinuing the drug (10, 55, 56). The assumption has been that the chronic use of the drug was producing a headache, which was temporarily relieved by taking another dose of the drug. Payne (51) has described what he considers withdrawal symptoms after prolonged administration of acetanilid in 2 dogs. He also mentions withdrawal symptoms in a series of patients, but a complete report on these has not been identified. A few clinical reports claim physical withdrawal signs, but evidence of physical dependence is lacking in the majority of reports. The basis for a drug headache is not clear. Sohler et al. (57) observed no dilatation of the pial blood vesels by acetanilid. Hanzlik (10) has suggested in connection with acetanilid that anemia, methemoglobinemia and sulfhemoglobinemia may be factors. Unpublished experimental studies on pain free human subjects have so far not indicated the development of either psychic or physical dependence (58, 59).

Barbiturates. It is a matter of general experience that hypnotic doses of the barbiturates produce little analgesia. Large doses, of course, have some effect in obtunding pain. In this connection, Wolff, Hardy, and Goodell (50) observed that when subjects were given 0.5 gram of evipal the sedative and hypnotic effects of the drug were evident within 20 minutes, and the subjects became relaxed, lethargic, unsteady on their feet, and slightly loquacious. Mental and mechanical abilities were depressed. However, in contrast to these rather marked sedative effects the pain threshold was elevated only about 20 per cent. This again emphasizes the fact that the analgesic action of the barbiturates is weak as compared to their sedative action.

The ability of the barbiturates to produce a sense of euphoria is apparently quite variable depending upon both the individual and the circumstances. As ordinarily employed for sedation and hypnosis euphoria is a minor factor.

In Tatum's review of the barbiturates (13) he states that the repeated and continued use of these drugs induces a condition of habituation or psychic dependence but apparently not a true addiction as exemplified by the use of morphine.

On the other hand, Schmidt (60) has described what he considers to be withdrawal symptoms in 11 epileptic patients who had taken phenobarbital for 6 years or more. Robinson (61) has reported a number of cases of chronic poisoning with barbturates in which on withdrawal there was evidence of strong psychic dependence, but he did not observe evidence of physical dependence except as indicated by increased irritability. Recently Kalinowsky (44) has described generalized convulsive seizures occurring 4 or 5 days after withdrawal of sodium barbital in 7 mentally disturbed non-epileptic patients who had been kept under continuous sedation for a year and one-half or longer. No subsequent seizures were observed during 3 years of observation. He also reported that the convulsive threshold to electric shock therapy was lowered after withdrawal of barbital medication. Tatum and Seevers (62) have recorded the development of withdrawal seizures in dogs after prolonged barbital medication. Oettel and Krautwald (63) observed that barbital and phenobarbital produced a degree of tolerance to the depressant effects together with a marked increase in reflex excitability, but this hyperirritability was not increased on withdrawal. Tolerance and hyperirritability but not abstinence symptoms were developed to phanodorn and nostal. Weiss (64) and Robinson (61) have discussed the problem of chronic barbiturate intoxication and stressed the possibility of irreparable damage to the brain and other tissue cells. This would be a condition in man more or less analogous to those described for the dog by Seevers and Tatum (62). They reported that in chronic barbital intoxication covering a period of over 3 years that there were well marked morphological changes in the brains as well as changes in deportment (see 62, 13, 61 for further discussion). They also noted evidence of a partial tolerance which has been confirmed by numerous other investigators (62) except Swanson, Weaver, and Chen (65). Tolerance to the hypnotic and sedative action of the barbiturates is sufficient according to Robinson (61) to require larger and larger doses which may often lead to evidence of clinical toxicity. Cross-tolerance between alcohol and some of the barbiturates has been demonstrated in the rabbit by Ahlquist and Dille (66).

Trichlorethylene is frequently inhaled for its analgesic effect. Wolff, Hardy and Goodell (50) have observed that when 1 cc. of the drug was inhaled there was a prompt elevation of the cutaneous pain threshold reaching a maximum elevation of 40 to 45 per cent in 15 minutes which was sustained for 9 to 20 minutes, and remained above the control level for about three quarters of an hour. During the inhalation, the subjects experienced sensations of "light-headedness" and impending syncope. A threshold raising effect was also noted on the hand as had earlier observers (67). Rubinstein and co-workers (68, 69) [illegible] the analgesic effect is due to central

actions since inhalation of the prescribed amount may produce stage I anesthesia. Giddiness, sleepiness, and even transient unconsciousness have been observed and occasionally lassitude, nausea, and palpitation. Chronic industrial poisoning with neuropathies have been reported (70, 71). Repeated use of trichlorethylene for inebriation and elation has been reported (72, 73).

Ergotamine tartrate has proved very effective in certain cases of migraine headache (74, 75). It has been demonstrated that the decline in the intensity of a headache is coincident with a decrease in the amplitude of pulsations of the cranial arteries (74). It has been supposed that this represents its mechanism of action. Wolff, Hardy, and Goodell (50) were unable to demonstrate any threshold raising effect of the drug. The psychological effects of ergotamine are frequently unpleasant, and tolerance apparently does not develop to its therapeutic effectiveness.

Caffeine is frequently combined with analgesics or used alone in the treatment of certain types of headache. Therefore, it is desirable to know if caffeine has any true analgesic action. In a small series of experiments (50) no effect was observed on the cutaneous pain threshold, although the usual psychic effect of increased alertness, well being, and general effectiveness was present. Evidence of a vasoconstrictor action on the cranial arteries has been observed (75, 76, 77, 78) which may be a factor in relieving certain headaches in a manner similar to that suggested for ergotamine (75, 78). Caffeine has been found effective in post lumbar puncture headache (78) and occasionally effective in migraine headache (75, 78).

Tolerance to the cerebral stimulant action of caffeine has not been conclusively demonstrated. Some measure of habituation is apparent although this does not necessarily involve psychi- dependence.

Caffeine withdrawal headache has been pro duced experimentally by Dreisbach (79) who note an accompanying change in blood electrolytes Von Storch (78) has suggested that this type o headache may be a result of vasodilitation follow ing prolonged vasoconstriction of the crania arteries (but see 80).

Considering the non-opiate analgesics in genera it appears that some separation of the euphoric analgesic, and physical dependence effects o drugs is possible. The clearest separation i evident in the analgesic-antipyretic group of drug in which a limited degree of analgesia is produce without euphoria, and thus far with practicall no evidence of physical dependence. Ergotamin and caffeine represent a special case in that th mechanism of analgesia is largely restricted t certain vascular effects. The analgesic an euphoric effects of the barbiturates and, to som extent, trichlorethylene are secondary to thei general cerebral depressant action. With alcoho euphoria and analgesia are more accentuated i relation to cerebral depression. Dependence o alcohol and the barbiturates is chiefly psychic bu evidence is accumulating to indicate a physiologi cal basis for establishment of some degree o physical dependence. The evidence so far indicates that of the drugs considered only demerol combines a potent analgesic action with euphoria and liability to physical dependence in any degree similar to that seen with the opiates.

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IV. WITH REFERENCE TO PHYSICAL DEPENDENCE

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The correct answer to this question cannot be given with assurance until the physiologic bases for these pharmacologic effects are clarified. While almost everyone has at some time experienced pharmacologic relief of pain, and perhaps also improvement in mood, relatively few have experienced or come to appreciate the reality of physical dependence on a drug. Since orientation is a necessary preliminary to discussion of physical dependence, it seems advisable to attempt to define it and present a concept of its nature before considering this aspect of the important question posed by Dr. Oberst.

Physical dependence is an arbitrary term used to denote the presence of an acquired abnormal state wherein the regular administration of adequate amounts of a drug has, through previous prolonged use, become requisite to physiologic equilibrium. Since it is not yet possible to diagnose physical dependence objectively without withholding drugs, the sine qua non of physical dependence remains the demonstration of a charac-

teristic abstinence syndrome. When persons have so received or abused a phenanthrene derivative of opium that physical dependence has resulted, after withholding the drug a definite group of signs and symptoms appear. Some of the phenomena which constitute the opiate abstinence syndrome are: yawning, lacrimation, rhinorrhea, perspiration, goose flesh, tremor, dilated pupils, anorexia, nausea, emesis, diarrhea, restlessness, insomnia, weight loss, dehydration, hyperglycemia, elevation of temperature and blood pressure, and alteration of the pulse rate. Many of these are, or could be manifestations of disturbances in function of the vegetative nervous system (1). Another indication for their autonomic origin lies in the fact that deprivation phenomena are characteristically uniform and predictable, and not influenced appreciably by the patient's attitude or reaction to the withdrawal. These observations together with the studies of DeBodo and co-workers (2), Brooks et al. (3), Hambourger (4), and Herrmann (5) indicating that morphine probably achieves certain of its important effects through action in the region of the hypothalamus, have led to the formulation of a working concept of the nature of physical dependence (by the Lexington group)[1] as being a condition of autonomic hyperreaction to opiates. This concept is based on the following points:

1. The prime function of autonomic (hypothalamic) centers is to maintain homeostasis and to make proper adjustments in the face of stress.
2. Morphine affects homeostasis through its action on these centers.
3. Autonomic reaction to this effect takes place. (Biological reactions generally are greater than necessary to overcome an effect.)
4. With repetition the ability to offset the opiate effect improves. (Physiological tolerance.)
5. An extension of this process of improved reaction results eventually (with larger and more frequent dosage) in disproportionate autonomic strength in checks and balances.
6. Thus a condition is created wherein a chemical is needed to maintain homeostasis; such reactive power having been developed that to preserve equilibrium there must be present an effect to counteract.
7. Since the body is unable to supply a counter-effect promptly it must be furnished from without, else equilibrium will be lost temporarily. Such loss of equilibrium results in an abstinence syndrome. Following subsidence of this spectacular illness, as much as six months of total abstinence may be required to regain optimum steady states (6).

If this concept be true, it is believed that it may be possible to separate analgesia and physical dependence, and perhaps also euphoria and physical dependence.

The euphoria obtained from morphine is thought to be due to a reduction in the "alarm" reaction through depression of autonomic centers. Morphine euphoria probably does not occur in normal pain-free subjects, but dysphoria is generally noted. On the other hand persons in whom homeostasis is disturbed easily are often uncomfortable. They may escape such discomfort in several ways: 1, by learning to lead simpler existences, thus reducing the frequency and intensity of disturbing stimuli; 2, by modifying the impact of such stimuli or the reaction thereto with drugs, or 3, outlets such as hobbies, exercises, psychosis, or other mechanism. An escape from discomfort is pleasant, and the resultant sense of well being is a form of euphoria. Euphoria from opiates probably results from reduced autonomic reaction to stimuli disturbing to homeostasis, and reduction in reception and/or perception of such stimuli. If these concepts of opiate euphoria and of opiate physical dependence be true, the two phenomena are scarcely separable. However, euphoria may be accomplished by mechanisms other than reduction in autonomic reaction to discomfort. Such agents as benzedrine, cocaine, aliphatic narcotics and hypnotics, and cannabis may improve mood through different pharmacological actions, and none of these is thought to cause clinically recognized physical dependence. This may be because of incomplete study for a caffeine abstinence syndrome has been described (7). Improved mood may also be achieved through proper indulgence in, or appreciation of hobbies, exercise, art, music, literature and other things for which the physiologic basis is not yet entirely clear. Thus, while drugs capable of causing physical dependence as described may inevitably have a beneficial effect on disturbed mood, euphoria can be achieved without accompanying physical dependence.

Analgesia represents relief of pain and of reactions to pain. Relief of pain entails a reduction of peripheral reception, neural transmission, perception of painful stimuli, or any combination. Peripheral reception may be reduced by local anesthetics, "coal-tar" analgetic agents, and salicylates; neural transmission may be reduced in the region of the thalamus, perhaps by morphine or demerol; and perception may be reduced by aliphatic narcotics and hypnotics.

The importance of relief of reactions to pain has been brought to the attention of the medical world through the work of Wolff, Hardy and Goodell (8). This aspect of morphine action probably entails depression of autonomic centers, hence may be part and parcel of the same process as opiate euphoria and physical dependence.

[1] To be presented at the A.A.A.S. Symposium of Drug Intoxication and Addiction, when held.

However, Wolff, Hardy and Goodell (9) have shown also that acetylsalicylic acid and alcohol may accomplish the same therapeutic results as morphine. Here, while there would be some autonomic depression, the sense of well being or reduction of "alarm" reaction probably is the result of cortical depression and the physiological influence of this on autonomic reactions. Then too, it may be that pain reception and perception are reduced more effectively by this combination than by morphine, thus lessening the stimuli which set off the "alarm" reaction. So far as is known, neither acetylsalicylic acid, alcohol, nor the combination causes physical dependence.

Another reason to continue to believe in the possibility of a separation of physical dependence and analgesia is that demerol seems to possess less physical dependence liability in proportion to its analgetic effectiveness than does morphine (10). Perhaps demerol has relatively greater thalamic and relatively less hypothalamic effect than morphine (?). While this new drug represents but a step in the right direction, it suggests that future developments in the field of synthetic substitutes may lead to ultimate realization of the goal of the Drug Addiction Committee of the National Research Council (11): A drug which will relieve pain effectively but not cause appreciable physical dependence.

In conclusion, it appears that while it is not yet possible to give a categorical answer to the question, "Can Euphoric, Analgetic, and Physical Dependence Effects of Drugs be Separated?" there are indications that such possibilities exist. The need for further work in the field of synthetic substitutes for morphine and for establishing the physiologic bases for these effects are obvious.

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(1) Himmelsbach, C. K. Ann. Int. Med. **15**: 829, 1941. (2) De Bodo, R. C., F. W. Co Tui and A. E. Benaglia. J. Pharmacol. and Exper. Therap. **61**: 48, 1937. de Bodo, R. C. and C. McC. Brooks. J. Pharmacol. and Exper. Therap. **61**: 82, 1937. (3) Brooks, C. McC., R. A. Goodwin and H. M. Willard. Am. J. Physiol. **133**: P 226, 1941. (4) Hambourger, W. E. Proc. Soc. Exper. Biol. and Med. **36**: 36, 1937; J. Pharmacol. and Exper. Therap. **69**: 289, 1940. (5) Herrmann, J. B. J. Pharmacol. and Exper. Therap. **72**: 130, 1941; **76**: 309, 1942. (6) Himmelsbach, C. K. Arch. Int. Med. **69**: 766, 1942. (7) Dreisbach, R. H. J. Pharmacol. and Exper. Therap. **69**: 283, 1940. Dreisbach, R. H. and C. Pfeiffer. J. Lab. and Clin. Med., **28**: 1212, 1943. (8) Wolff, H. G., J. D. Hardy and H. Goodell. J. Clin. Investigation **19**: 659, 1940. (9) Wolff, H. G., J. D. Hardy and H. Goodell. J. Pharmacol. and Exper. Therap. **75**: 38, 1942. (10) Himmelsbach, C. K. J. Pharmacol. and Exper. Therap. **75**: 64, 1942. (11) Small, L. F., N. B. Eddy, E. Mossetig and C. K. Himmelsbach. Supp. no. 138 to the P. H. R., 1938.

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY

No Federation Meeting in 1944. Executive Committee for the second time decides not to project a meeting because of conditions incident to the prosecution of the War.

In a mail-vote recorded October 1, 1943 the Executive Committee, because of restrictions on civilian travel and other conditions incident to the full prosecution of the war, decided (9-2) not to project a meeting of the Federation at Cleveland in 1944. In a similar earlier vote (October 23, 1942) the Committee had decided to hold the first post-war Federation meeting in Cleveland. While the present vote (not to project a Federation meeting in 1944) was being canvassed the Cleveland Local Committee reported that circumstances would make it inexpedient to attempt to entertain the whole Federation at one time in 1944.

These decisions do not, of course, preclude the holding of individual meetings by the constituent societies of the Federation in Cleveland or elsewhere.

In connection with the foregoing decision the Executive Committee at the same time voted (10-1) to publish a third volume of the Federation Proceedings in 1944, patterned after the second volume of which this is the last issue.

The next (March) issue of the Proceedings will therefore contain abstracts of current research reports supplied by the members in accordance with notices to be sent out by the secretaries of the constituent societies. The June and September issues will be available for the publication of symposium papers, as heretofore, and the last issue (December 1944) will carry the membership list and other material, as in this issue.

EXECUTIVE COMMITTEE, 1943

PHILIP BARD, WALLACE O. FENN, The Physiological Society

RUDOLPH J. ANDERSON, ARNOLD K. BALLS, The Biochemical Society

E. K. MARSHALL, JR., RAYMOND N. BIETER, The Pharmacological Society

BALDUIN LUCKÉ, H. P. SMITH, The Pathological Society

H. B. LEWIS, ARTHUR H. SMITH, The Institute of Nutrition

JACQUES J. BRONFENBRENNER, ARTHUR F. COCA, The Association of Immunologists

PHILIP BARD, *Chairman*, Johns Hopkins Medical School, Baltimore, Md.

ALBERT G. HOGAN, *Ex-Chairman*

D. R. HOOKER, *Secretary*, 19 W. Chase St., Baltimore, Md.

STANDING COMMITTEES

Defence of Biological Research: ELLIOTT C. CUTLER, *Chairman;* A. B. LUCKHARDT, C. I. REED, G. H. WHIPPLE.

International Congresses: H. S. GASSER, Physiology, *Chairman;* A. J. CARLSON, Physiology; D. D. VAN SLYKE, Biochemistry; E. K. MARSHALL, JR., Pharmacology; PEYTON ROUS, Pathology; L. A. MAYNARD, Nutrition; J. J. BRONFENBRENNER, Immunology.

Public Information: HARRY GOLDBLATT, *Chairman;* R. G. HOSKINS, R. W. GERARD.

Placement Service: H. B. LEWIS, *Director.*

Representatives, Council A.A.A.S.: G. PHILIP GRABFIELD, CHARLES G. KING.

Federation Proceedings, Control Committee: PHILIP BARD, *Chairman;* C. G. KING, MORTON MCCUTCHEON, C. F. SCHMIDT, A. H. SMITH.

FORMER EXECUTIVE COMMITTEES

Philadelphia, Dec. 28-31, 1913

S. J. MELTZER, *Chairman*, and A. J. CARLSON, *Secretary*, The Physiological Society. A. B. MACALLUM and P. A. SHAFFER, The Biochemical Society. T. SOLLMANN and J. AUER, The Pharmacological Society.

St. Louis, Dec. 27-30, 1914

G. LUSK, *Chairman*, and P. A. SHAFFER, *Secretary*, The Biochemical Society. T. SOLLMANN and J. AUER, The Pharmacological Society. R. M. PEARCE and G. H. WHIPPLE, The Pathological Society. W. B. CANNON and A. J. CARLSON, The Physiological Society.

Boston, Dec. 26-29, 1915

TORALD SOLLMANN, *Chairman*, and JOHN AUER, *Secretary*, The Pharmacological Society. THEOBALD SMITH and PEYTON ROUS, The Pathological Society. W. B. CANNON and C. W. GREENE, The Physiological Society. WALTER JONES and P. A. SHAFFER, The Biochemical Society.

New York, Dec. 27–30, 1916

SIMON FLEXNER, *Chairman*, and PEYTON ROUS, *Secretary*, The Pathological Society. W. B. CANNON and C. W. GREENE, The Physiological Society. WALTER JONES and STANLEY R. BENEDICT, The Biochemical Society. REID HUNT and J. AUER, The Pharmacological Society.

Minneapolis-Rochester, Dec. 27–29, 1917

FREDERIC S. LEE, *Chairman*, and CHARLES W. GREENE, *Secretary*, The Physiological Society. CARL L. ALSBERG and STANLEY R. BENEDICT, The Biochemical Society. REID HUNT and L. G. ROWNTREE, The Pharmacological Society. LUDVIG HEKTOEN and HOWARD T. KARSNER, The Pathological Society.

Baltimore, April 24–26, 1918

CARL L. ALSBERG, *Chairman*, and STANLEY R. BENEDICT, *Secretary*, The Biochemical Society. REID HUNT and E. D. BROWN, The Pharmacological Society. H. GIDEON WELLS and HOWARD T. KARSNER, The Pathological Society. FREDERIC S. LEE and CHARLES W. GREENE, The Physiological Society.

Cincinnati, Dec. 29–31, 1919

A. S. LOEVENHART, *Chairman*, and E. D. BROWN, *Secretary*, The Pharmacological Society. W. G. MACCALLUM and HOWARD T. KARSNER, The Pathological Society. WARREN P. LOMBARD and CHARLES W. GREENE, The Physiological Society. STANLEY R. BENEDICT and VICTOR C. MYERS, The Biochemical Society.

Chicago, Dec. 28–30, 1920

WILLIAM H. PARK, *Chairman*, and HOWARD T. KARSNER, *Secretary*, The Pathological Society. WARREN P. LOMBARD and CHARLES W. GREENE, The Physiological Society. STANLEY R. BENEDICT and VICTOR C. MYERS, The Biochemical Society. A. S. LOEVENHART and EDGAR D. BROWN, The Pharmacological Society.

New Haven, Dec. 28–30, 1921

J. J. R. MACLEOD, *Chairman*, and CHARLES W. GREENE, *Secretary*, The Physiological Society. D. D. VAN SLYKE and VICTOR C. MYERS, The Biochemical Society. C. W. EDMUNDS and EDGAR D. BROWN, The Pharmacological Society. F. G. NOVY and WADE H. BROWN, The Pathological Society.

Toronto, Dec. 27–29, 1922

D. D. VAN SLYKE, *Chairman*, and VICTOR C. MYERS, *Secretary*, The Biochemical Society. C. W. EDMUNDS and EDGAR D. BROWN, The Pharmacological Society. HOWARD T. KARSNER and WADE H. BROWN, The Pathological Society. J. J. R. MACLEOD and CHARLES W. GREENE, The Physiological Society.

St. Louis, Dec. 27–29, 1923

C. W. EDMUNDS, *Chairman*, and EDGAR D. BROWN, *Secretary*, The Pharmacological Society. E. L. OPIE and WADE H. BROWN, The Pathological Society. A. J. CARLSON and CHARLES W. GREENE, The Physiological Society. PHILIP A. SHAFFER and VICTOR C. MYERS, The Biochemical Society.

Washington, Dec. 29–31, 1924

ALDRED S. WARTHIN, *Chairman*, and E. B. KRUMBHAAR, *Secretary*, The Pathological Society. A. J. CARLSON and WALTER J. MEEK, The Physiological Society. P. A. SHAFFER and D. WRIGHT WILSON, The Biochemical Society. JOHN AUER and E. D. BROWN, The Pharmacological Society.

Cleveland, Dec. 28–30, 1925

A. J. CARLSON, *Chairman*, and WALTER J. MEEK, *Secretary*, The Physiological Society. H. C. SHERMAN and D. WRIGHT WILSON, The Biochemical Society. JOHN AUER and E. D. BROWN, The Pharmacological Society. GEORGE H. WHIPPLE and E. B. KRUMBHAAR, The Pathological Society.

Rochester, N. Y., April 14–16, 1927

E. C. KENDALL, *Chairman*, and F. C. KOCH, *Secretary*, The Biochemical Society. JOHN AUER and E. D. BROWN, The Pharmacological Society. W. H. BROWN and E. B. KRUMBHAAR, The Pathological Society. J. ERLANGER and W. J. MEEK, The Physiological Society.

Ann Arbor, April 12–14, 1928

CARL VOEGTLIN, *Chairman*, and E. D. BROWN, *Secretary*, The Pharmacological Society. DAVID MARINE and CARL V. WELLER, The Pathological Society. JOSEPH ERLANGER and WALTER J. MEEK, The Physiological Society. E. V. MCCOLLUM and D. WRIGHT WILSON, The Biochemical Society.

Boston, Aug. 19–24, 1929

(The XIIIth International Physiological Congress)

EDWARD B. KRUMBHAAR, *Chairman*, and CARL V. WELLER, *Secretary*, The Pathological Society. JOSEPH ERLANGER and WALTER J. MEEK, The Physiological Society. E. V. MCCOLLUM and D. WRIGHT WILSON, The Biochemical Society. CARL VOEGTLIN and E. D. BROWN, The Pharmacological Society.

Chicago, March 26–29, 1930

WALTER J. MEEK, *Chairman*, and ALFRED C. REDFIELD, *Secretary*, The Physiological Society. W. R. BLOOR and HOWARD B. LEWIS, The Biochemical Society. CARL VOEGTLIN and E. D. BROWN, The Pharmacological Society. WILLIAM F. PETERSEN and CARL V. WELLER, The Pathological Society.

Montreal, April 8–11, 1931

W. R. BLOOR, *Chairman*, and H. B. LEWIS, *Secretary*, The Biochemical Society. GEORGE B. WALLACE and E. D. BROWN, The Pharmacological Society. FREDERICK L. GATES and C. PHILLIP MILLER, The Pathological Society. WALTER J. MEEK and ARNO B. LUCKHARDT, The Physiological Society.

Philadelphia, April 27–30, 1932

GEORGE B. WALLACE, *Chairman*, and V. E. HENDERSON, *Secretary*, The Pharmacological Society. SAMUEL R. HAYTHORN and C. PHILLIP MILLER, The Pathological Society. WALTER J. MEEK and ARNO B. LUCKHARDT, The Physiological Society. H. C. BRADLEY and HOWARD B. LEWIS, The Biochemical Society.

Cincinnati, April 10–12, 1933

PEYTON ROUS, *Chairman*, and C. PHILLIP MILLER, *Secretary*, The Pathological Society. ARNO B. LUCKHARDT and FRANK C. MANN, The Physiological Society. H. C. BRADLEY and HOWARD B. LEWIS, The Biochemical Society. WM. DEB. MACNIDER and V. E. HENDERSON, The Pharmacological Society.

New York, March 28–31, 1934

ARNO B. LUCKHARDT, *Chairman*, FRANK C. MANN, *Secretary*, and ALEXANDER FORBES, *Treasurer*, The Physiological Society. W. M. CLARK and H. A. MATTILL, The Biochemical Society. W. DEB. MACNIDER and V. E. HENDERSON, The Pharmacological Society. CARL V. WELLER and C. PHILLIP MILLER, The Pathological Society.

Detroit, April 10–13, 1935

W. M. CLARK, *Chairman*, H. A. MATTILL, *Secretary*, and C. H. FISKE, *Treasurer*, the Biochemical Society. CHARLES W. GREENE and FRANK C. MANN, The Physiological Society. R. A. HATCHER and E. M. K. GEILING, The Pharmacological Society. S. BURT WOLBACH and SHIELDS WARREN, The Pathological Society.

Washington, March 25–28, 1936

V. E. HENDERSON, *Chairman*, E. M. K. GEILING, *Secretary*, and C. M. GRUBER, *Treasurer*, The Pharmacological Society. FRANK C. MANN and ANDREW C. IVY, The Physiological Society. H. B. LEWIS and H. A. MATTILL, The Biochemical Society. OSKAR KLOTZ and SHIELDS WARREN, The Pathological Society.

Memphis, April 21–24, 1937

ALPHONSE R. DOCHEZ, *Chairman*, and SHIELDS WARREN, The Pathological Society. FRANK C. MANN and ANDREW C. IVY, The Physiological Society. HOWARD B. LEWIS and H. A. MATTILL, The Biochemical Society. V. E. HENDERSON and E. M. K. GEILING, The Pharmacological Society. D. R. HOOKER, *Secretary*.

Baltimore, March 30–April 2, 1938

WILLIAM T. PORTER, *Honorary President*; WALTER E. GARREY, *Chairman*, and ANDREW C. IVY, The Physiological Society. GLENN E. CULLEN and H. A. MATTILL, The Biochemical Society. ARTHUR L. TATUM and G. PHILIP GRABFIELD, The Pharmacological Society. C. PHILLIP MILLER and PAUL R. CANNON, The Pathological Society. D. R. HOOKER, *Secretary*.

Toronto, April 26–29, 1939

GLENN E. CULLEN, *Chairman*, and CHARLES G. KING, The Biochemical Society. ARTHUR L. TATUM and G. PHILIP GRABFIELD, The Pharmacological Society. C. PHILLIP MILLER and PAUL R. CANNON, The Pathological Society. WALTER E. GARREY and ANDREW C. IVY, The Physiological Society. D. R. HOOKER, *Secretary*.

New Orleans, March 13–16, 1940

E. M. K. GEILING, *Chairman*, and G. PHILIP GRABFIELD, The Pharmacological Society. ERNEST W. GOODPASTURE and PAUL R. CANNON, The Pathological Society. ANDREW C. IVY and PHILIP BARD, The Physiological Society. WILLIAM C. ROSE and CHARLES G. KING, The Biochemical Society. D. R. HOOKER, *Secretary*.

Chicago, April 15–19, 1941

SHIELDS WARREN, *Chairman*, and H. P. SMITH, The Pathological Society. THORNE M. CARPENTER and L. A. MAYNARD, The Institute of Nutrition. ANDREW C. IVY and PHILIP BARD, The Physiological Society. WILLIAM C. ROSE and CHARLES G. KING, The Biochemical Society. E. M. K. GEILING and G. PHILIP GRABFIELD, The Pharmacological Society. D. R. HOOKER, *Secretary*.

Boston, March 31, April 1, 2, 3, 4, 1942

ALBERT G. HOGAN, *Chairman*, and ARTHUR H. SMITH, The Institute of Nutrition. PHILIP BARD and CARL J. WIGGERS, The Physiological Society. RUDOLPH J. ANDERSON and ARNOLD K. BALLS, The Biochemical Society. E. M. K. GEILING and R. N. BIETER, The Pharmacological Society.

JESSE L. BOLLMAN and H. P. SMITH, The Pathological Society. SHIELDS WARREN, *Ex-Chairman.* D. R. HOOKER, *Secretary.*

1943: The meeting scheduled for Cleveland, April 6–10, was cancelled because of war conditions

PHILIP BARD, *Chairman,* and WALLACE O. FENN, The Physiological Society. RUDOLPH J. ANDERSON and ARNOLD K. BALLS, The Biochemical Society. E. K. MARSHALL, JR. and RAYMOND N. BIETER, The Pharmacological Society. BALDUIN LUCKÉ and H. P. SMITH, The Pathological Society. LEONARD A. MAYNARD and ARTHUR H. SMITH, The Institute of Nutrition. JACQUES J. BRONFENBRENNER and ARTHUR F. COCA, The Association of Immunologists.

BY-LAWS

BY-LAWS

Adopted at the Washington Meeting, 1936 and amended at the Boston Meeting, 1942

1. The Presidents and Secretaries of the Constituent Societies, the Chairman of the Executive Committee of the preceding year and the Federation Secretary shall form the Executive Committee of the Federation.

2. The Chairmanship of the Executive Committee shall be held in turn by the Presidents of the Constituent Societies, who shall succeed one another annually in the order of seniority of the Societies.

3. The Executive Committee shall appoint annually from the membership of the Federation a secretary-treasurer, to be known as the Federation Secretary.

4. The Federation Secretary shall: (a) Keep the minutes of the Executive Committee and distribute copies to the Secretaries of the Constituent Societies. (b) Make arrangements for the Annual Meeting with the Local Committee, with the approval of the Executive Committee. (c) Print in convenient combined form and distribute to the membership of the Federation the programs of the Constituent Societies as received from their respective Secretaries. (d) Undertake such other duties, to be decided upon from time to time by the Executive Committee, as do not conflict with the complete autonomy of the Constituent Societies.

5. The Executive Committee shall control all monies in the hands of the Federation Secretary, who shall make an annual report to the Executive Committee for audit and approval. The expenses of the Federation Secretary, as authorized by the Executive Committee, shall be the first charge on such monies and if insufficient for the purpose the Executive Committee shall prorate such expenses to the Constituent Societies of the Federation in proportion to their respective memberships.

The Executive Committee may appropriate Federation monies annually for the uses of Local Committees and for the uses of other authorized Committees but in the latter cases an audit of expenditures shall be made and approved before such committees are discharged.

6. The Executive Committee shall determine the place of the Annual Meeting, and the time shall be determined by the Local Committee, preferably within the period of March fifteenth to May first.

7. The local Committee at the place of meeting of the Federation shall charge such fee for registration as may be approved by the Executive Committee. The monies thus collected shall be used to defray the expenses of the Local Committee and the remainder, after such expenses have been met, shall be turned over to the Federation Secretary.

8. The Executive Committee shall consider measures of advantage to the Federation as a whole. Any Constituent Society may refer similar measures to the Executive Committee. No action, however, shall be taken by the Executive Committee unless specifically authorized by all the Constituent Societies.

9. The Chairman of the Executive Committee may appoint committees when the purposes of such committees have been approved by all the Constituent Societies of the Federation. Such committees shall be appointed for a term of one year, but may be continued and their members reappointed. Such committees shall report in writing to the Executive Committee, which shall in turn report thereon to the Constituent Societies either for information or recommendation. The Secretaries of the Constituent Societies shall report the recommendations of their respective Societies to the Executive Committee for final action.

10. All individuals whose names appear on the program by invitation or introduction and those registering from any recognized biological laboratory may be enrolled as Associate Members of the Federation for that Annual Meeting. Such Associate Members may enjoy all the privileges of the Annual Meeting except that of voting.

11. No person may present orally more than one paper during all of the scientific sessions of the Constituent Societies at the time of the Annual Meeting except upon invitation of the Executive Committee or a Council. Papers must be submitted to the Secretary of the Society of which the proposer is a member. The proposer may request transfer to another program, but this may only

be done with the consent of the Secretary of the Society concerned. Any Secretary who regards any paper submitted to him as better suited to the program of another Society may arrange this transfer with the Secretary of the Society concerned, if it be possible. Such transfer shall be indicated on the program.

12. Abstracts not to exceed two hundred and fifty words in length, of papers approved for presentation at all of the scientific sessions of all the Constituent Societies at the Annual Meeting, shall receive publication in the *Federation Proceedings*.

13. A Control Committee, consisting of at least one representative of each Constituent Society as designated by the several Councils, shall have editorial control over the *Federation Proceedings* which shall be financed as required by an annual assessment of all the members of each Constituent Society.

14. The Control Committee shall have power to choose certain additional papers presented at the Annual Meetings and from other sources, including material heretofore published in the Federation Yearbook, for publication in the Federation Proceedings.

PLACEMENT SERVICE

The Federation maintains a service to act as a medium of communication between persons seeking positions for teaching or research and institutions that wish to fill vacancies in these sciences.

The service does not undertake to recommend or to pass judgment upon applicants. It aims merely to serve as a clearing-house for such information as above stated and to bring into touch with one another candidates for positions and vacancies to be filled.

Persons, whether members of the Federation or not, and institutions desiring to avail themselves of the service, may receive such information as is available without cost to the applicant.

All communications should be addressed to Dr. H. B. Lewis, Director, University of Michigan, Ann Arbor, Mich.

THE AMERICAN PHYSIOLOGICAL SOCIETY

Founded December 30, 1887; Incorporated June 2, 1923

OFFICERS ELECTED 1942

President—PHILIP BARD, Johns Hopkins School of Medicine, Baltimore, Md.

Secretary—WALLACE O. FENN, University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Treasurer—HALLOWELL DAVIS, Harvard University School of Medicine, Boston, Mass.

Council—PHILIP BARD, WALLACE O. FENN, HALLOWELL DAVIS, CHARLES H. BEST, University of Toronto, Canada, MAURICE B. VISSCHER, University of Minnesota, Minneapolis, HIRAM E. ESSEX, Mayo Foundation, Rochester, Minn., W. F. HAMILTON, University of Georgia, Augusta.

Board of Publication Trustees—WALTER J. MEEK, HENRY C. BAZETT, ANDREW C. IVY.

PAST OFFICERS

Organization Meeting, December 30, 1887

S. WEIR MITCHELL, *President*
H. N. MARTIN, *Secretary*

1888 H. P. BOWDITCH, President; H. N. MARTIN, Secretary-Treasurer; J. G. CURTIS, H. C. WOOD, H. SEWALL, Councilors. 1889 S. WEIR MITCHELL, President; H. N. MARTIN, Secretary-Treasurer; H. P. BOWDITCH, J. G. CURTIS, H. C. WOODS, Councilors. 1890 S. WEIR MITCHELL, President; H. N. MARTIN, Secretary-Treasurer; H. P. BOWDITCH, J. G. CURTIS, H. H. DONALDSON, Councilors. 1891 H. P. BOWDITCH, President; H. N. MARTIN, Secretary-Treasurer; R. H. CHITTENDEN, J. G. CURTIS, H. H. DONALDSON, Councilors. 1892 H. P. BOWDITCH, President; H. N. MARTIN, Secretary-Treasurer; R. H. CHITTENDEN, J. G. CURTIS, W. H. HOWELL, Councilors. 1893 H. P. BOWDITCH, President; W. P. LOMBARD, Secretary-Treasurer; R. H. CHITTENDEN, J. G. CURTIS, W. H. HOWELL, Councilors. 1894 H. P. BOWDITCH, President; W. P. LOMBARD, Secretary-Treasurer; R. H. CHITTENDEN, W. H. HOWELL, J. W. WARREN, Councilors. 1895 H. P. BOWDITCH, President; F. S. LEE, Secretary-Treasurer; R. H. CHITTENDEN, W. H. HOWELL, W. P. LOMBARD, Councilors. 1896 R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; H. P. BOWDITCH, W. H. HOWELL, J. W. WARREN, Councilors. 1897 R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; H. P. BOWDITCH, W. H. HOWELL, W. P. LOMBARD, Councilors. 1898 R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; H. P. BOWDITCH, W. H. HOWELL, W. P. LOMBARD, Councilors. 1899 R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; W. H. HOWELL, W. P. LOMBARD, W. T. PORTER, Councilors. 1900 R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; W. H. HOWELL, W. P. LOMBARD, W. T. PORTER, Councilors. 1901

R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; W. H. HOWELL, W. P. LOMBARD, W. T. PORTER, Councilors. **1902** R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; W. H. HOWELL, W. P. LOMBARD, W. T. PORTER, Councilors. **1903** R. H. CHITTENDEN, President; F. S. LEE, Secretary-Treasurer; W. H. HOWELL, W. P. LOMBARD, W. T. PORTER, Councilors. **1904** R. H. CHITTENDEN, President; W. T. PORTER, Secretary-Treasurer; F. S. LEE, W. P. LOMBARD, W. H. HOWELL, Councilors. **1905** W. H. HOWELL, President; L. B. MENDEL, Secretary; W. B. CANNON, Treasurer; R. H. CHITTENDEN, S. J. MELTZER, Councilors. **1906** W. H. HOWELL, President; L. B. MENDEL, Secretary; W. B. CANNON, Treasurer; A. B. MACALLUM, S. J. MELTZER, Councilors. **1907** W. H. HOWELL, President; L. B. MENDEL, Secretary; W. B. CANNON, Treasurer; J. J. ABEL, G. LUSK, Councilors. **1908** W. H. HOWELL, President; R. HUNT, Secretary; W. B. CANNON, Treasurer; J. J. ABEL, G. LUSK, Councilors. **1909** W. H. HOWELL, President; R. HUNT, Secretary; W. B. CANNON, Treasurer; A. J. CARLSON, W. P. LOMBARD, Councilors. **1910** W. H. HOWELL, President; A. J. CARLSON, Secretary; W. B. CANNON, Treasurer; J. ERLANGER, F. S. LEE, Councilors. **1911** S. J. MELTZER, President; A. J. CARLSON, Secretary; W. B. CANNON, Treasurer; J. ERLANGER, F. S. LEE, Councilors. **1912** S. J. MELTZER, President; A. J. CARLSON, Secretary; W. B. CANNON, Treasurer; J. ERLANGER, F. S. LEE, Councilors. **1913** S. J. MELTZER, President; A. J. CARLSON, Secretary; J. ERLANGER, Treasurer; W. B. CANNON, F. S. LEE, Councilors. **1914** W. B. CANNON, President; A. J. CARLSON, Secretary; J. ERLANGER, Treasurer; F. S. LEE, S. J. MELTZER, Councilors. **1915** W. B. CANNON, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; W. E. GARREY, W. H. HOWELL, J. J. R. MACLEOD, W. J. MEEK, Councilors. **1916** W. B. CANNON, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; W. E. GARREY, W. H. HOWELL, J. J. R. MACLEOD, W. J. MEEK, Councilors. **1917** F. S. LEE, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; W. B. CANNON, W. H. HOWELL, J. J. R. MACLEOD, W. J. MEEK, Councilors. **1918** F. S. LEE, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; W. B. CANNON, W. H. HOWELL, J. J. R. MACLEOD, W. J. MEEK, Councilors. **1919** W. P. LOMBARD, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; W. B. CANNON, Y. HENDERSON, J. J. R. MACLEOD, W. J. MEEK, Councilors. **1920** W. P. LOMBARD, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; W. B. CANNON, J. J. R. MACLEOD, Y. HENDERSON, C. J. WIGGERS, Councilors. **1921** J. J. R. MACLEOD, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; J. A. E. EYSTER, Y. HENDERSON, C. J. WIGGERS, A. J. CARLSON, Councilors. **1922** J. J. R. MACLEOD, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; Y. HENDERSON, C. J. WIGGERS, A. J. CARLSON, J. A. E. EYSTER, Councilors. **1923** A. J. CARLSON, President; C. W. GREENE, Secretary; J. ERLANGER, Treasurer; C. J. WIGGERS, A. B. LUCKHARDT, J. A. E. EYSTER, J. R. MURLIN, Councilors. **1924** A. J. CARLSON, President; W. J. MEEK, Secretary; C. K. DRINKER, Treasurer; A. B. LUCKHARDT, J. A. E. EYSTER, J. R. MURLIN, W. E. GARREY, Councilors. **1925** A. J. CARLSON, President; W. J. MEEK, Secretary; C. K. DRINKER, Treasurer; J. A. E. EYSTER, J. R. MURLIN, W. E. GARREY, JOSEPH ERLANGER, Councilors. **1926** J. ERLANGER, President; W. J. MEEK, Secretary; A. FORBES, Treasurer; J. R. MURLIN, W. E. GARREY, A. B. LUCKHARDT, C. J. WIGGERS, Councilors. **1927** J. ERLANGER, President; W. J. MEEK, Secretary; A. FORBES, Treasurer; W. E. GARREY, A. B. LUCKHARDT, C. J. WIGGERS, R. GESELL, Councilors. **1928** J. ERLANGER, President; W. J. MEEK, Secretary; A. FORBES, Treasurer; A. B. LUCKHARDT, C. J. WIGGERS, R. GESELL, A. J. CARLSON, Councilors. **1929** W. J. MEEK, President; ALFRED C. REDFIELD, Secretary; A. FORBES, Treasurer; C. J. WIGGERS, R. GESELL, A. J. CARLSON, J. R. MURLIN, Councilors. **1930** W. J. MEEK, President; ARNO B. LUCKHARDT, Secretary; A. FORBES, Treasurer; R. GESELL, A. J. CARLSON, J. R. MURLIN, E. G. MARTIN, Councilors. **1931** W. J. MEEK, President; ARNO B. LUCKHARDT, Secretary; ALEXANDER FORBES, Treasurer; A. J. CARLSON, J. R. MURLIN, E. G. MARTIN, JOHN TAIT, Councilors. **1932** ARNO B. LUCKHARDT, President; FRANK C. MANN, Secretary; ALEXANDER FORBES, Treasurer; E. G. MARTIN, W. J. MEEK, J. R. MURLIN, JOHN TAIT, Councilors. **1933** ARNO B. LUCKHARDT, President; FRANK C. MANN, Secretary; ALEXANDER FORBES, Treasurer; HERBERT S. GASSER, ERNEST G. MARTIN, W. J. MEEK, JOHN TAIT, Councilors. **1934** CHARLES W. GREENE, President; FRANK C. MANN, Secretary; ALEXANDER FORBES, Treasurer; HERBERT S. GASSER, ARNO B. LUCKHARDT, W. J. MEEK, JOHN TAIT, Councilors. **1935** FRANK C. MANN, President; ANDREW C. IVY, Secretary; ALEXANDER FORBES, Treasurer; CHARLES H. BEST, HERBERT S. GASSER, ARNO B. LUCKHARDT, W. J. MEEK, Councilors. **1936** FRANK C. MANN, President; ANDREW C. IVY, Secretary; WALLACE O. FENN, Treasurer; CHARLES H. BEST, PHILIP BARD, HERBERT S. GASSER, ARNO B. LUCKHARDT, Councilors. **1937** WALTER E. GARREY, President; ANDREW C. IVY, Secretary; WALLACE O. FENN, Treasurer; CHARLES H. BEST, PHILIP BARD, HERBERT S. GASSER, ARNO B. LUCKHARDT, Councilors. **1938** WILLIAM T. PORTER, Honorary

President; WALTER E. GARREY, President; ANDREW C. IVY, Secretary; WALLACE O. FENN, Treasurer; ARNO B. LUCKHARDT, CHARLES H. BEST, PHILIP BARD, HERBERT S. GASSER, Councilors. 1939 ANDREW C. IVY, President; PHILIP BARD, Secretary; WALLACE O. FENN, Treasurer; CHARLES H. BEST, HERBERT S. GASSER, ARNO B. LUCKHARDT, MAURICE B. VISSCHER, Councilors. 1940 ANDREW C. IVY, President; PHILIP BARD, Secretary; CARL J. WIGGERS, Treasurer; CHARLES H. BEST, HERBERT S. GASSER, ARNO B. LUCKHARDT, MAURICE B. VISSCHER, Councilors. 1941 PHILIP BARD, President; CARL J. WIGGERS, Secretary; HALLOWELL DAVIS, Treasurer; CHARLES H. BEST, ARNO B. LUCKHARDT, MAURICE B. VISSCHER, HIRAM E. ESSEX, Councilors. 1942 PHILIP BARD, President; WALLACE O. FENN, Secretary; HALLOWELL DAVIS, Treasurer; CHARLES H. BEST, MAURICE B. VISSCHER, HIRAM E. ESSEX, W. F. HAMILTON, Councillors.

CONSTITUTION

I

1. This Society shall be named "THE AMERICAN PHYSIOLOGICAL SOCIETY."

2. The Society is instituted to promote the advance of Physiology and to facilitate personal intercourse between American Physiologists.

II

1. The Society shall consist of ordinary and of honorary members.

2. Any person who has conducted and published original researches in Physiology, and who is a resident of North America, shall be eligible for election as an ordinary member of the Society.

3. Distinguished men of science who have contributed to the advance of Physiology shall be eligible for election as honorary members of the Society. Honorary members shall pay no membership fee. They shall have the right of attending the meetings of the Society, and of taking part in its scientific discussions, but they shall have no vote.

III

1. The management of the Society shall be vested in a Council consisting of the President, Secretary, Treasurer, and four other members to be chosen from the ordinary members by ballot at each annual meeting. The President, Secretary, and Treasurer shall be elected for one year. The President shall be subject to only one reëlection. The four additional members of the Council shall be elected for a term of four years, and the term of office of one of these councilors shall expire at the close of each annual meeting. He or she shall not be eligible for reëlection for a period of two years.

2. The Council shall have power to fill such vacancies as may occur in its membership or in any committee of the Society unless the vacancy is produced by a resignation presented at a meeting.

IV

1. At least a fortnight before the annual meeting the Secretary shall send to each member a notice of the place and time of each meeting, and shall make such other announcements as the Council shall direct.

2. The annual assessment shall be determined by the Council, and shall be due in advance at the time of the annual meeting. Beyond the ordinary expenditures required by the duties of the Secretary and Treasurer, no money of the Society shall be disbursed save by authority of the Council.

3. Any member whose assessment is two years in arrears shall cease to be a member of the Society, unless at the next annual meeting he shall be reinstated by special vote of the Society; and it shall be the duty of the Treasurer to inform the Secretary that he may notify the said delinquent of his right to appeal to said meeting.

4. Any member who has paid the annual assessment for thirty years, or who has attained the age of sixty-five years, or who has retired because of illness, may be relieved from the payment of the annual assessment.

V

1. The annual meeting of the Society shall be held at a time and place determined by the Council in consultation with the Executive Committee of the Federation of American Societies for Experimental Biology.

2. Special meetings may be held at such times and places as the Council may determine.

VI

1. Proposed changes in the Constitution must be sent in writing to the Secretary at least one month before the date of the meeting at which they are to be considered, and must be signed by at least three ordinary members. The Secretary shall send a printed copy of any proposed change to each ordinary member at least two weeks before the next meeting.

2. If at this meeting two-thirds of the votes cast shall favor the proposed change, it shall be made.

3. At all annual meetings of the Society ten ordinary members shall form a quorum for the transaction of business.

VII

1. The Council may, from the names of the candidates proposed in writing by at least two ordinary

members of the Society, nominate candidates for election to ordinary membership. The names of the candidates so nominated, together with the names of their proposers and a statement of their qualifications for membership, shall be posted on a bulletin board at an annual meeting of the Society. The candidates may be balloted for at any session of the same meeting, and one black ball in eight shall exclude.

2. Honorary members shall be proposed by the Council, and shall be elected by ballot of the members present at an annual meeting and one negative vote in twenty shall exclude.

VIII

If a majority of the Council shall decide that the interests of the Society require the expulsion of a member, the Secretary shall send a notice of this decision to each ordinary member at least two weeks before the next annual meeting. At this meeting the Secretary shall, on behalf of the Council, propose the expulsion; and if two-thirds of the members present vote for it, the member shall be expelled, his assessment for the current year shall be returned to him, and he shall cease to be a member of the Society.

IX

1. The official organs of the Society shall be the *American Journal of Physiology* and such other Journals as the Society shall from time to time establish. These the Society shall own and manage.

2. The management of the *Journals* shall be vested in the Council. The Council shall make a full report to the Society at each annual meeting of the financial condition and the publication policy of the *Journals*.

BY-LAWS

1. All papers read before the Society shall be limited to a length of ten minutes. No person may orally present more than one paper. In case of joint authorship the name of the individual who will orally present the paper shall stand first.

2. Abstracts in duplicate, not to exceed two-hundred and fifty words in length, of all papers to be presented at the Annual Meeting of the Society shall be required by the Secretary for publication in the Federation Proceedings, in accordance with rules approved by the Council.

3. The Council may, upon the request of ten ordinary members, call a special meeting of the Society, at any time and place, for the reading of papers and the promotion of personal intercourse. Such meetings shall be held in accordance with the Constitution and By-Laws of the Society; and if the regular officers of the Society are not present, the members in attendance shall elect a temporary Chairman and Secretary. The latter officer shall forward an account of the scientific proceedings of the meeting to the offical Secretary of the Society for insertion in the minutes; he shall also prepare and transmit to the official Secretary such abstracts of papers read as may be furnished him, and these abstracts shall be published in the *Federation Proceedings* in accordance with By-Law 2.

THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, INCORPORATED

Founded December 6, 1906; Incorporated September 12, 1919

OFFICERS ELECTED 1943

President—E. A. Doisy, St. Louis University School of Medicine, St. Louis 4, Mo.

Vice-President—A. B. Hastings, Harvard Medical School, Boston, Mass.

Secretary—A. K. Balls, U. S. Bureau of Agricultural and Industrial Chemistry, Western Regional Research Laboratory, Albany 6, California.

Treasurer—W. C. Stadie, Maloney Clinic, University of Pennsylvania, Philadelphia, Pa.

Councilors-at-large—W. C. Rose, University of Illinois, Urbana, Ill.; H. T. Clarke, Columbia University, New York City; R. J. Anderson, Sterling Laboratory, Yale University, New Haven, Conn.

Nominating Committee—D. D. Van Slyke, Chairman, G. O. Burr, H. B. Lewis, H. B. Vickery, W. M. Clark, C. L. A. Schmidt, W. R. Bloor, H. A. Mattill, C. F. Cori.

PAST OFFICERS

1907 Russell H. Chittenden, President; J. J. Abel, Vice-President; W. J. Gies, Secretary; L. B. Mendel, Treasurer; W. Jones, W. Koch, J. Marshall, T. B. Osborne, Councilors. 1908 John J. Abel, President; Otto Folin, Vice-President; Wm. J. Gies, Secretary; L. B. Mendel, Treasurer; A. B. Macallum, A. P. Mathews, F. G. Novy, Councilors. 1909 Otto Folin, President; T. B. Osborne, Vice-President; Wm. J. Gies, Secretary; L. B. Mendel, Treasurer; J. J. Abel, P. A. Levene, G. Lusk, Councilors. 1910 Thomas B. Osborne, President; L. B. Mendel, Vice-President; A. N. Richards, Secretary; Walter Jones, Treasurer; A. B. Macallum, A.

P. MATHEWS, V. C. VAUGHAN, Councilors. 1911 LAFAYETTE B. MENDEL, President; A. B. MACALLUM, Vice-President; A. N. RICHARDS, Secretary; WALTER JONES, Treasurer; WM. J. GIES, A. S. LOEVENHART, P. A. SHAFFER, Councilors. 1912 ARCHIBALD B. MACALLUM, President; G. LUSK, Vice-President; A. N. RICHARDS, Secretary; WALTER JONES, Treasurer; H. P. ARMSBY, L. B. MENDEL, H. G. WELLS, Councilors. 1913 ARCHIBALD B. MACALLUM, President; G. LUSK, Vice-President; P. A. SHAFFER, Secretary; D. D. VAN SLYKE, Treasurer; H. P. ARMSBY, L. B. MENDEL, H. G. WELLS, Councilors. 1914 GRAHAM LUSK, President; C. L. ALSBERG, Vice-President; P. A. SHAFFER, Secretary; D. D. VAN SLYKE, Treasurer; J. J. ABEL, A. B. MACALLUM, T. B. OSBORNE, Councilors. 1915 WALTER JONES, President; C. L. ALSBERG, Vice-President; P. A. SHAFFER, Secretary; D. D. VAN SLYKE, Treasurer; OTTO FOLIN, G. LUSK, L. B. MENDEL, Councilors. 1916 WALTER JONES, President; F. P. UNDERHILL, Vice-President; S. R. BENEDICT, Secretary; D. D. VAN SLYKE, Treasurer; OTTO FOLIN, A. B. MACALLUM, P. A. SHAFFER, Councilors. 1917 CARL L. ALSBERG, President; A. P. MATHEWS, Vice-President; S. R. BENEDICT, Secretary; H. C. BRADLEY, Treasurer; L. J. HENDERSON, P. A. SHAFFER, F. P. UNDERHILL, Councilors. 1918 CARL L. ALSBERG, President; A. P. MATHEWS, Vice-President; S. R. BENEDICT, Secretary; H. C. BRADLEY, Treasurer; W. J. GIES, ANDREW HUNTER, E. V. MCCOLLUM, Councilors. 1919 STANLEY, R. BENEDICT, President; D. D. VAN SLYKE, Vice-President; V. C. MYERS, Secretary; H. C. BRADLEY, Treasurer; ANDREW HUNTER, E. V. MCCOLLUM, L. B. MENDEL, Councilors. 1920 STANLEY R. BENEDICT, President; D. D. VAN SLYKE, Vice-President; V. C. MYERS, Secretary; H. C. BRADLEY, Treasurer; OTTO FOLIN, WALTER JONES, L. B. MENDEL, Councilors. 1921 DONALD D. VAN SLYKE, President; P. A. SHAFFER, Vice-President; V. C. MYERS, Secretary; H. C. BRADLEY, Treasurer; S. R. BENEDICT, OTTO FOLIN, WALTER JONES, Councilors. 1922 DONALD D. VAN SLYKE, President; P. A. SHAFFER, Vice-President; V. C. MYERS, Secretary; W. R. BLOOR, Treasurer; S. R. BENEDICT, H. C. BRADLEY, A. P. MATHEWS, Councilors. 1923 PHILIP A. SHAFFER, President; H. C. SHERMAN, Vice-President; V. C. MYERS, Secretary; W. R. BLOOR, Treasurer; H. C. BRADLEY, ANDREW HUNTER, A. P. MATHEWS, Councilors. 1924 PHILIP A. SHAFFER, President; HENRY C. SHERMAN, Vice-President; D. WRIGHT WILSON, Secretary; WALTER R. BLOOR, Treasurer; OTTO FOLIN, ANDREW HUNTER, VICTOR C. MYERS, Councilors. 1925 HENRY C. SHERMAN, President; EDWARD C. KENDALL, Vice-President; D. WRIGHT WILSON, Secretary; WALTER R. BLOOR, Treasurer; OTTO FOLIN, LAFAYETTE B. MENDEL, PHILIP A. SHAFFER, Councilors. 1926 EDWARD C. KENDALL, President; ELMER V. MCCOLLUM, Vice-President; FRED C. KOCH, Secretary; GLENN E. CULLEN, Treasurer; J. B. COLLIP, EDWARD A. DOISY, ALBERT P. MATHEWS, Councilors. 1927 E. V. MCCOLLUM, President; W. R. BLOOR, Vice-President; D. WRIGHT WILSON, Secretary; G. E. CULLEN, Treasurer; E. A. DOISY, F. C. KOCH, D. D. VAN SLYKE, Councilors. 1928 E. V. MCCOLLUM, President; W. R. BLOOR, Vice-President; D. WRIGHT WILSON, Secretary; G. E. CULLEN, Treasurer; WM. M. CLARK, F. C. KOCH, D. D. VAN SLYKE, Councilors. 1929 W. R. BLOOR, President; H. C. BRADLEY, Vice-President; H. B. LEWIS, Secretary; G. E. CULLEN, Treasurer; W. M. CLARK, C. L. A. SCHMIDT, P. A. SHAFFER, Councilors. 1930 W. R. BLOOR, President; H. C. BRADLEY, Vice-President; H. B. LEWIS, Secretary; G. E. CULLEN, Treasurer; W. M. CLARK, P. A. SHAFFER, D. W. WILSON, Councilors. 1931 H. C. BRADLEY, President; W. M. CLARK, Vice-President; H. B. LEWIS, Secretary; C. H. FISKE, Treasurer; W. C. ROSE, P. A. SHAFFER, D. W. WILSON, Councilors. 1932 H. C. BRADLEY, President; W. M. CLARK, Vice-President; H. B. LEWIS, Secretary; C. H. FISKE, Treasurer; P. E. HOWE, W. C. ROSE, D. W. WILSON, Councilors. 1933 W. M. CLARK, President; H. B. LEWIS, Vice-President; H. A. MATTILL, Secretary; C. H. FISKE, Treasurer; H. C. BRADLEY, P. E. HOWE, W. C. ROSE, Councilors. 1934 W. M. CLARK, President; H. B. LEWIS, Vice-President; H. A. MATTILL, Secretary; C. H. FISKE, Treasurer; H. C. BRADLEY, E. A. DOISY, P. E. HOWE, Councilors. 1935 H. B. LEWIS, President; G. E. CULLEN, Vice-President; H. A. MATTILL, Secretary; C. H. FISKE, Treasurer; H. C. BRADLEY, J. B. COLLIP, E. A. DOISY, Councilors. 1936 H. B. LEWIS, President; G. E. CULLEN, Vice-President; H. A. MATTILL, Secretary; A. B. HASTINGS, Treasurer; J. B. COLLIP, E. A. DOISY, W. C. ROSE, Councilors. 1937 G. E. CULLEN, President; W. C. ROSE, Vice-President; H. A. MATTILL, Secretary; A. B. HASTINGS, Treasurer; E. A. DOISY, H. B. LEWIS, H. B. VICKERY, Councilors. 1938 G. E. CULLEN, President; W. C. ROSE, Vice-President; CHARLES G. KING, Secretary; A. B. HASTINGS, Treasurer; H. B. LEWIS, H. A. MATTILL, H. B. VICKERY, Councilors. 1939 W. C. ROSE, President; R. J. ANDERSON, Vice-President; CHARLES G. KING, Secretary; A. B. HASTINGS, Treasurer; H. B. LEWIS, H. A. MATTILL, G. E. CULLEN, Councilors. 1940 WILLIAM C. ROSE, President; RUDOLPH J. ANDERSON, Vice-President; CHARLES G. KING, Secretary; A. B. HASTINGS, Treasurer; H. A. MATTILL, GLENN E. CULLEN, E. A. DOISY, Councilors. 1941 R. J. ANDERSON, President; E. A. DOISY, Vice-President; A. K. BALLS, Secretary; W. C. STADIE, Treasurer; H. B. LE C.

ROSE, Councilors. 1942 R. J. ANDERSON, President; E. A. DOISY, Vice-President; A. K. BALLS, Secretary; W. C. STADIE, Treasurer; W. C. ROSE, C. A. KING, H. Y. CLARKE, Councilors.

CONSTITUTION

FROM THE ARTICLES OF INCORPORATION

1. The name of the proposed corporation is "AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, INCORPORATED."

2. The purposes for which this corporation is formed are to further the extension of biochemical knowledge and to facilitate personal intercourse between American investigators in biological chemistry.

BY-LAWS

ARTICLE I.—*Membership*

SECTION 1. *Eligibility for Membership.*—Qualified investigators who have conducted and published meritorious original investigations in biological chemistry shall be eligible for membership in the Society.

SEC. 2. *Nomination.*—Nominations for membership shall be made and seconded by members of the Society on blanks furnished by the Secretary. Nominations shall be submitted to the Council who shall determine eligibility and make recommendation to the Society at a regular meeting.

SEC. 3. *Election to Membership.*—A. A nominee for membership may be voted for by ballot at any meeting of the Society after Council has reported its findings on his eligibility. The eligible candidate shall be reported by the Council as "eligible" or as "eligible and indorsed." B. A majority of the ballots cast shall elect.

SEC. 4. *Forfeiture.*—A. Any member who may grant the use of his name for (a) the advertisement of a patent medicine, a proprietary food preparation, or any other commercial article of doubtful value to the public or possibly harmful to the public health, or (b) who may concede its use for the purpose of encouraging the sale of individual samples (of any such product) that he has not examined, shall forfeit his membership.

B. The Council shall have authority to announce forfeiture of membership, provided that the copy of the charges, together with a written notice of a hearing thereon by the Council at a place and time specified in such notice, shall have been delivered to the member charged with violating the preceding section either personally or mailed to him at his last known address at least thirty days before the date of such hearing.

SEC. 5. *Expulsion.*—Upon the recommendation of the Council any member may be expelled by a majority vote of the total membership at a meeting of the Society, provided that a copy of the charges against him, together with a written notice of a hearing thereon by the Council at a place and time specified in such notice shall have been delivered to him personally or mailed to him at his last known address at least thirty days before the date of such hearing.

ARTICLE II.—*Meetings and Quorum*

SECTION 1. *Annual.*—The annual meeting of the Society shall be held on the date fixed by the Certificate of Incorporation.

SEC. 2. *Special.*—A special meeting may be called at any time by the President, or in case of his absence or disability, by the Vice-President, and must be called at the request of a majority of the Council or fifteen members of the Society. A notice specifying the purpose of such meeting shall be mailed to each member at least ten days previous thereto. The Council shall select the places at which meetings shall be held.

SEC. 3. *Quorum.*—Fifteen members shall constitute a quorum at all meetings of the Society, but in absence of a quorum any number shall be sufficient to adjourn to a fixed date.

ARTICLE III.—*Officials*

SECTION 1. *Officers.*—The officers shall be a President, a Vice-President, a Secretary, and a Treasurer, who shall be elected annually by the members of the Society.

SEC. 2. *Council.*—A. The officers so elected and three additional members, one of whom shall be elected at each annual meeting of the Society to serve a three year term, shall constitute the Board of Directors of the corporation and shall be known as "The Council." (When this provision is first put into effect three members will need to be elected for a one, a two and a three year period.)

B. No two members of the Council may be from the same institution, and none of the officers so elected shall be eligible for re-election for more than two years except the Secretary and Treasurer, who shall be eligible for re-election for five years. The three additional members of the Council shall be ineligible for re-election (until after the lapse of one year).

SEC. 3. *Duties of Officers.*—The powers and duties of the officers elected by the Society shall be such as usually devolve upon their respective positions.

SEC. 4. *Assistant Treasurer.*—A. The Council may from time to time appoint a trust company, or some member of the Society, to serve during the pleasure of the Council as Assistant Treasurer, and to act as depositary of the investments and income of the "Christian A. Herter Memorial Fund" and of such other funds as the Society may from time to time commit to its or his charge.

B. The Assistant Treasurer shall have and exercise the following powers and duties, viz., the

custody and safe-keeping of securities and cash belonging to the "Christian A. Herter Fund" and the collection of income and other moneys due to the Fund, with power to receipt for the same and to endorse for deposit all checks payable to the Society or the Treasurer, or to the Journal of Biological Chemistry for income or other moneys due to the Fund, the investment or reinvestment of the capital of the Fund, subject to the approval of the Council; the disbursement of principal under the direction of the Council and the disbursement of income under the direction of the Editorial Board of the Journal of Biological Chemistry, such disbursement to be made under a resolution of the Council or Board, or with the approval of two members of either the Council or Board, as the case may be. The Assistant Treasurer shall keep books of account and render statments, annually or oftener upon the request of the Council or Board setting forth the condition of the Fund and the recepits and disbursements since the date of the preceding statement.

ARTICLE IV.—*The Council*

SECTION 1. *Powers.*—The general management of the Society during the intervals between meetings shall be vested in the Council, which shall regularly perform the ordinary duties of an executive committee and possess all the powers conferred upon the Board of Directors of a membership corporation by the Membership Corporation Law of the State of New York.

SEC. 2. *Reports.*—The Council shall report to the Society as promptly as possible its findings on the eligibility of candidates for membership, and on all charges of a violation of these By-Laws.

SEC. 3. *Journal of Biological Chemistry.*—The Council shall have power to appoint the persons to act as proxies for the Society at all meetings of the stockholders of the "Journal of Biological Chemistry" (a corporation) of which all the stock is owned by the Society, and also to designate the persons to be elected as Directors of such corporation.

SEC. 4. *Herter Fund.*—It shall be the duty of the Council to see that the "Christian A. Herter Memorial Fund" is administered in accordance with the terms of the Trust Agreement, dated May 16, 1911, executed by the Journal of Biological Chemistry and the donors of said Fund.

ARTICLE V.—*Nominating Committee*

SECTION 1. *Membership.*—A. The Nominating Committee shall consist of nine members from nine different institutions elected at each annual meeting to serve for the ensuing year. Members who have served on the Nominating Committee for two consecutive years shall be ineligible for re-election until after the lapse of one year.

B. The member of the Nominating Committee who is elected to the Committee by the largest number of votes shall become Chairman and Secretary of the Committee.

SEC. 2. *Nomination of Officials.*—A. The Nominating Committee shall make at least one nomination for each of the four offices and for each of the three additional positions in the Council to be filled by vote of the members.

B. The nominations by the Nominating Committee must be transmitted to the Secretary at least one month before the annual meeting at which they are to be considered.

C. The Secretary shall send to every member, at least two weeks before the annual meeting, two copies of the list of nominees presented to him by the Nominating Committee and at the same time shall notify all the members that they may vote by proxy.

D. At the opening of the first executive session of the ensuing annual meeting the Secretary shall formally present the regular nominations for the Nominating Committee.

E. Additional nominations for the offices and for membership in the Council may be made by any member at the opening of the first executive session of any annual meeting.

F. Nominations for membership on the Nominating Committee shall be made by or for individual members, either in person or by proxy, and not otherwise, at the opening of the first executive session of any annual meeting.

SEC. 3. *Election of Officials.*—A. The Secretary shall receive and present to the tellers, appointed by the President to take charge of the election, all signed ballots forwarded by absent members. When such ballots are presented to the tellers the Secretary shall announce the names of the members voting by proxy, and he shall record the same names in the minutes of the meeting.

B. All elective officials shall be selected by ballot at the close of the first executive session of each annual meeting.

C. A majority of the votes cast shall be necessary to elect an official.

D. Elective officials shall take office on July 1st following the annual meeting.

SEC. 4. *Filling of Vacancies.*—A. The Nominating Committee shall fill all vacancies in elective positions except such as may occur at a meeting of the Society.

B. The President of the Society shall fill all vacancies in appointive positions.

ARTICLE VI.—*Financial*

SECTION 1. *Dues.*—Annual assessments shall be determined by majority vote at the annual meetings, upon the recommendation of the Council, and shall be due January 15th in each year.

Members who have reached the age of 65 years, or who have become incapacitated, may, by vote of the Council, be exempted from the payment of dues.

SEC. 2. *Expenditures.*—No expenditures from the general funds of the Society except those required in the performance of the ordinary official duties shall be made except by vote of the Society or the Council, but this section shall not apply to expenditures from the "Christian A. Herter Memorial Fund."

SEC. 3. *Privileges of Membership Begin with Payment of Dues.*—Candidates for membership, if elected, shall not be entitled to any of the privileges of membership, before they pay the dues of the fiscal year succeeding their election.

SEC. 4. *Penalty for Non-Payment of Dues.*—A. Members in arrears for dues for a period of three consecutive years shall thereupon forfeit their membership.

B. Delinquent members may be reinstated by the Council provided all indebtedness to the Society is liquidated.

SEC. 5. *Herter Fund.*—The "Christian A. Herter Memorial Fund" shall be held and invested separately from the general funds of the Society and the income thereof shall be expended under the direction of the Editorial Board exclusively for the maintenance and support of the Journal of Biological Chemistry, subject to the supervision and control of the Editorial Committee in accordance with the terms of the Trust Agreement mentioned in ARTICLE IV, SECTION 4, and the provisions of ARTICLE VII of the By-Laws.

ARTICLE VII.—*Journal of Biological Chemistry*

SECTION 1. *Editorial Committee.*—There shall be an Editorial Committee consisting of nine members of the Society who shall be nominated by the Nominating Committee and elected by the Society in the same manner as officers. The nine members first elected shall divide themselves by lot into three classes of three in each class, to serve for two, four, and six years respectively, and thereafter three members shall be elected at each alternate annual meeting of the Society to succeed the members of the outgoing class and to serve for a term of six years. Members of the Committee shall be eligible to re-election.

SEC. 2. *Powers of Committee.*—The Committee shall have power to elect an Editorial Board and shall have final authority in matters pertaining to the general policy of the Journal.

SEC. 3. *Editorial Board.*—The members of the Board shall hold office until their successors are elected and shall appoint a Managing Editor from among their own number who shall have direct responsibility and authority for the active editorial conduct of the Journal, and who shall have discretionary power in arranging the details as to the conduct of the Journal. The expenditures of the income of the "Christian A. Herter Memorial Fund" shall be under the direction of the Board, and the approval of any two members of the Board shall be a sufficient warrant to authorize payments from such income.

ARTICLE VIII.—*Papers on Scientific Subjects*

SECTION 1. *Presentation of Papers.*—The Secretary shall request each member who signifies his intention of reading a paper at any session to specify the length of time which its presentation will require. The time thus specified shall be printed on the official program, and the presiding officer shall have no authority to extend it unless a majority of the members present signify their wish to the contrary. In the absence of any specification of time required not more than ten minutes shall be allotted for the reading of any one paper.

SEC. 2. *Number of Papers.*—No member shall be permitted to present more than one paper, either alone or in collaboration, until every member shall have had the opportunity of presenting one paper.

ARTICLE IX.—*Corporate Seal*

SECTION 1. The corporate seal of the corporation shall be a circle surrounded by the words, "AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS," and including the word, "INCORPORATED."

ARTICLE X.—*Amendments*

SECTION 1. *Amendments.*—These By-Laws, after having been approved by the Council, and adopted by the Society at its first annual meeting, shall not be amended except as hereinafter provided.

SEC. 2. *Manner of Presentation.*—Proposed amendments to the By-Laws must be sent to the Secretary at least one month before the date of the meeting at which they are to be considered and must be indorsed in writing by at least three members.

SEC. 3. *Notice of Intended Amendments.*—The Secretary shall give every member notice of proposed amendments at least two weeks before the meeting at which they are to be considered and shall notify all members that they may vote by proxy.

SEC. 4. *Adoption of Amendments.*—A. The Secretary shall receive and present to the tellers appointed by the President all signed ballots forwarded by absent members. When such ballots are presented to the tellers, the Secretary shall announce the names of members voting by proxy, and he shall record the same names in the minutes of the meeting.

B. Votes upon amendments shall be cast at the opening of the second executive session of the meeting at which they are considered.

C. Affirmative votes from three-fifths of the members voting shall be required for the adoption of an amendment.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, INCORPORATED

Founded December 28, 1908; Incorporated June 19, 1933

OFFICERS ELECTED 1942

President—E. K. MARSHALL, JR., The Johns Hopkins School of Medicine, Baltimore, Maryland.

Vice-President—CARL A. DRAGSTEDT, Northwestern University Medical School, Chicago, Illinois.

Secretary—RAYMOND N. BIETER, University of Minnesota Medical School, Minneapolis.

Treasurer—E. E. NELSON, Burroughs, Wellcome & Co., Experimental Research Laboratories, Tuckahoe, N. Y.

Council—McK. CATTELL, Cornell University Medical College, New York, New York, R. G. SMITH, Tulane University, New Orleans, La., E. K. MARSHALL, JR., C. A. DRAGSTEDT, R. N. BIETER, E. E. NELSON.

Membership Committee—HARRY GOLD (term expires 1943), Cornell University Medical College, New York, New York, M. H. SEEVERS (term expires 1944), University of Michigan, Ann Arbor, Michigan, HARVEY B. HAAG (term expires 1945), Medical College of Virginia, Richmond, Virginia.

Nominating Committee—H. O. CALVERY, Chairman, A. C. DEGRAFF, J. M. DILLE, B. H. ROBBINS, F. F. YONKMAN.

PAST OFFICERS

1909 J. J. ABEL, President; REID HUNT, Secretary; A. S. LOEVENHART, Treasurer; S. J. MELTZER, T. SOLLMANN, C. W. EDMUNDS, A. C. CRAWFORD, Councilors. 1910 J. J. ABEL, President; REID HUNT, Secretary; A. S. LOEVENHART, Treasurer; A. C. CRAWFORD, G. B. WALLACE, Councilors. 1911 J. J. ABEL, President; REID HUNT, Secretary; A. S. LOEVENHART, Treasurer; G. B. WALLACE, W. DEB. MACNIDER, Councilors. 1912 J. J. ABEL, President; J. AUER, Secretary; A. S. LOEVENHART, Treasurer; G. B. WALLACE, REID HUNT, Councilors. 1913 T. SOLLMANN, President; J. AUER, Secretary; A. S. LOEVENHART, Treasurer; J. J. ABEL, W. DEB. MACNIDER, Councilors. 1914 T. SOLLMANN, President, J. AUER, Secretary; W. DEB. MACNIDER, Treasurer; J. J. ABEL, A. S. LOEVENHART, Councilors. 1915 T. SOLLMANN, President; J. AUER, Secretary; W. DEB. MACNIDER, Treasurer; WORTH HALE, D. E. JACKSON, Councilors. 1916 REID HUNT, President; J. AUER, Secretary; W. DEB. MACNIDER, Treasurer; A. D. HIRSCHFELDER, G. B. ROTH, Councilors. 1917 REID HUNT, President; L. G. ROWNTREE, Secretary; W. DEB. MACNIDER, Treasurer; J. AUER, CARL VOEGTLIN, Councilors. 1918 REID HUNT, President; E. D. BROWN, Secretary; W. DEB. MACNIDER, Treasurer; HUGH MCGUIGAN, CARL VOEGTLIN, Councilors. 1919 A. S. LOEVENHART, President; E. D. BROWN, Secretary; W. DEB. MACNIDER, Treasurer; REID HUNT, E. K. MARSHALL, JR., Councilors. 1920 A. S. LOEVENHART, President; E. D. BROWN, Secretary; W. DEB. MACNIDER, Treasurer; D. E. JACKSON, E. K. MARSHALL, JR., Councilors. 1921 C. W. EDMUNDS, President; E. D. BROWN, Secretary; HUGH MCGUIGAN, Treasurer; JOHN AUER, J. P. HANZLIK, Councilors. 1922 C. W. EDMUNDS, President; E. D. BROWN, Secretary; HUGH MCGUIGAN, Treasurer; J. P. HANZLIK, H. G. BARBOUR, Councilors. 1923 C. W. EDMUNDS, President; E. D. BROWN, Secretary; HUGH MCGUIGAN, Treasurer; J. P. HANZLIK, H. G. BARBOUR, Councilors. 1924 JOHN AUER, President; E. D. BROWN, Secretary; A. L. TATUM, Treasurer; J. P. HANZLIK, H. G. BARBOUR, Councilors. 1925 JOHN AUER, President; E. D. BROWN, Secretary; A. L. TATUM, Treasurer; H. G. BARBOUR, W. DEB. MACNIDER, Councilors. 1926 JOHN AUER, President; E. D. BROWN, Secretary; A. L. TATUM, Treasurer; H. G. BARBOUR, W. DEB. MACNIDER, Councilors. 1927 CARL VOEGTLIN, President; E. D. BROWN, Secretary; A. L. TATUM, Treasurer; V. E. HENDERSON, C. W. EDMUNDS, Councilors. 1928 CARL VOEGTLIN, President; E. D. BROWN, Secretary; A. L. TATUM, Treasurer; V. E. HENDERSON, C. W. EDMUNDS, Councilors. 1929 CARL VOEGTLIN, President; E. D. BROWN, Secretary; O. H. PLANT, Treasurer; V. E. HENDERSON, C. W. EDMUNDS, Councilors. 1930 GEORGE B. WALLACE, President; E. D. BROWN, Secretary; O. H. PLANT, Treasurer; H. G. BARBOUR, C. M. GRUBER, Councilors. 1931 GEORGE B. WALLACE, President; VELYIEN E. HENDERSON, Secretary; O. H. PLANT, Treasurer; PAUL D. LAMSON, WILLIAM DEB. MACNIDER, Councilors. 1932 WM. DEB. MACNIDER, President; A. N. RICHARDS, Vice-President; V. E.

HENDERSON, Secretary; O. H. PLANT, Treasurer; G. B. ROTH, A. L. TATUM, Councilors. **1933** WM. DEB. MACNIDER, President; A. L. TATUM, Vice-President; V. E. HENDERSON, Secretary; O. H. PLANT, Treasurer; C. M. GRUBER, G. B. ROTH, Councilors. **1934** R. A. HATCHER, President; A. L. TATUM, Vice-President; E. M. K. GEILING, Secretary; O. H. PLANT, Treasurer; WM. DEB. MACNIDER, R. L. STEHLE, Councilors. **1935** V. E. HENDERSON, President; O. H. PLANT, Vice-President; E. M. K. GEILING, Secretary; C. M. GRUBER, Treasurer; FLOYD DE EDS, M. S. DOOLEY, Councilors. **1936** V. E. HENDERSON, President; O. H. PLANT, Vice-President; E. M. K. GEILING, Secretary; C. M. GRUBER, Treasurer; C. W. EDMUNDS, G. B. WALLACE, Councilors. **1937** A. L. TATUM, President; E. M. K. GEILING, Vice-President; G. P. GRABFIELD, Secretary; C. M. GRUBER, Treasurer; V. E. HENDERSON, M. H. SEEVERS, Councilors. **1938** A. L. TATUM, President; E. M. K. GEILING, Vice-President; G. P. GRABFIELD, Secretary; C. M. GRUBER, Treasurer; E. K. MARSHALL, JR., C. F. SCHMIDT, Councilors. **1939** O. H. PLANT, President; E. M. K. GEILING, Vice-President; G. P. GRABFIELD, Secretary; E. E. NELSON, Treasurer; A. L. TATUM, C. A. DRAGSTEDT, Councilors. **1940** E. M. K. GEILING, President; C. F. SCHMIDT, Vice-President; G. PHILIP GRABFIELD, Secretary; E. E. NELSON, Treasurer; B. H. ROBBINS, C. H. THIENES, Councilors. **1941** E. M. K. GEILING, President; C. F. SCHMIDT, Vice-President; RAYMOND N. BIETER, Secretary; E. E. NELSON, Treasurer; E. G. GROSS, R. G. SMITH, Councilors. **1942** E. K. MARSHALL, JR., President; CARL A. DRAGSTEDT, Vice-President; RAYMOND N. BIETER, Secretary; E. E. NELSON, Treasurer; McK. CATTELL, R. G. SMITH, Councilors.

CONSTITUTION

ARTICLE I.—*Name*

The name of this organization shall be the "AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, INCORPORATED."

ARTICLE II.—*Objects*

The purpose of this Society shall be to promote these branches of science and to facilitate personal intercourse between investigators who are actively engaged in research in these fields.

ARTICLE III.—*Membership*

SECTION 1. Any person who has conducted and published a meritorious investigation in pharmacology or experimental therapeutics, and who is an active investigator in one of these fields, shall be eligible to membership, subject to the conditions of the other sections of Article III.

SEC. 2. A. Candidates for membership to this Society shall be proposed by two members who are not members of the Council. The names so proposed shall be sent to the Secretary at least three months prior to the Annual Meeting.

B. The Membership Committee shall investigate the qualifications of the candidates and report to the Council.

C. Candidates reported upon by the Membership Committee to the Council may be recommended for admission by the Council only provided they have been unanimously approved by both the Membership Committee and the Council.

D. The names of the candidates recommended for admission by the Council shall be posted by the Secretary not later than the day preceding the election for members.

E. The election of members shall be by individual ballot; one opposing vote in every eight cast shall be sufficient to exclude a candidate from membership.

SEC. 3. *Forfeiture of Membership.*

A. Any member whose assessment is three years in arrears shall cease to be a member of the Society, unless he shall be reinstated by a special vote of the Council; and it shall be the duty of the Treasurer to inform the Secretary that he may notify the said delinquent of his right to appeal to the Council.

B. If the Council shall decide that it is for the best interests of the Society that a member be expelled, the member shall be notified and given an opportunity of a hearing before the Council. Upon the recommendation of the Council the member then may be expelled by a three-fourths vote of those present at a regular meeting of the Society.

SEC. 4. *Honorary Members.*

A. Distinguished men of science who have contributed to the advance of pharmacology or experimental therapeutics shall be eligible for election as honorary members of the Society.

B. Nominations for honorary members shall take the same course as nominations for ordinary members (Art. III, Sec. 2); but their election shall require the unanimous vote of the members present at the election.

C. Honorary members shall pay no membership fee. They shall have the right to attend all meetings of the Society, and to take part in its discussions, but they shall have no vote.

D. The conditions for continuation of membership shall be the same for honorary as for ordinary members (Art. III, Sec. 3), except that forfeiture for arrears of fees does not apply to honorary members.

ARTICLE IV.—*Officers and Elections*

SECTION 1. The management of the Society shall be vested in a Council of six officers, consisting of

a President, a Vice President, a Secretary, a Treasurer, and two additional members.

SEC. 2. There shall be a Membership Committee consisting of three members, and a Nominating Committee consisting of five members. No two members of either Committee shall be from the same institution.

SEC. 3. Members of the Council shall serve for one year but they shall be eligible for re-election.

SEC. 4. The election of the Membership Committee shall be held annually at the time when the election of officers occurs. At the first meeting of the Society under this Constitution, one member shall be elected to serve on the Committee for three years, one for two years, and one for one year; and subsequently one member shall be elected each year to serve for a period of three years.

SEC. 5. A. Members of the Nominating Committee shall serve for one year. They are eligible for re-election, but shall not hold membership in the Committee for more than two consecutive years.

B. The Nominating Committee shall make at least one nomination for each office and for position on the Membership Committee to be filled by vote of the members. The nominations so made shall be transmitted to the Secretary and by him in turn to the members, at least one month before the annual meeting. Additional nominations may be made by any member at the time of the annual meeting.

C. Nominations for membership on the Nominating Committee shall be made by individual members at the time of the annual election. The five nominees who receive the highest number of votes shall be declared elected. The Nominating Committee shall select its own chairman who shall also serve as secretary to the Committee.

SEC. 6. The election of officers shall be held at the close of the first session of the annual meeting. In voting there shall be a ballot in regular order for each office to be filled, and the majority of the votes cast shall be necessary to a choice.

SEC. 7. Such vacancies as may occur in the offices and in the various committees in the interval between annual meetings shall be filled by a majority vote of the Council.

ARTICLE V.—*Meetings*

SECTION 1. The annual meeting of the Society shall be held at a time and place determined by the Council in consultation with the Executive Committee of the Federation of American Societies for Experimental Biology.

SEC. 2. Special meetings may be held at such times and places as the Council may determine.

SEC. 3. At least four weeks before the annual meeting the Secretary shall send to each member a notice of the time and place of such meeting and shall make such announcements as the Council may direct.

ARTICLE VI.—*Financial*

SECTION 1. The annual assessment shall be determined by majority vote at the annual meetings, upon the recommendation of the Council, and shall be due in advance at the time of the meeting.

SEC. 2. Beyond the ordinary expenditures required by the routine business of the Society no money shall be disbursed save by the authority of the Council or Society.

SEC. 3. The treasurer shall make an annual report to the Society.

SEC. 4. In case any profits result to the Society from the Journal of Pharmacology and Experimental Therapeutics at the end of the financial year, such profits shall be kept in a special account, after deducting any sums expended by the Society during the year for the conduct of the Journal, and shall be held subject to the order of the Council on recommendation of the Editorial Board.

ARTICLE VII.—*Quorum*

Ten members shall constitute a quorum for the transaction of business.

ARTICLE VIII.—*By-Laws*

By-Laws shall be adopted, altered or repealed at any meeting by two-thirds vote of the ballots cast.

ARTICLE IX.—*Amendments*

SECTION 1. Intended amendments to the Constitution shall be sent to the Secretary at least one month before the date of the meeting at which they are to be considered, and must be indorsed in writing by at least three members.

SEC. 2. The Secretary shall give all members due notice of proposed amendments.

SEC. 3. A four-fifths vote of the members present shall be required for the adoption of an amendment.

ARTICLE X.—*Journal*

SECTION 1. The official publication of the Society shall be the Journal of Pharmacology and Experimental Therapeutics.

SEC. 2. The Society shall elect an Editor-in-Chief for a term of three years and he with the approval of the Council shall appoint an Editorial Board of six members for a term of three years.

SEC. 3. The Editorial Board shall have direct authority and responsibility for the active editorial conduct of the Journal of Pharmacology and Experimental Therapeutics and shall have discretionary power in arranging details as to the conduct of the Journal.

BY-LAWS

1. Papers to be read shall be selected by the President and Secretary, who shall be empowered to arrange the program in their discretion. Papers not read shall appear on the program as read by title. No member shall be permitted to read or have read by title more than one paper.

2. An abstract of a paper to be read before the Society shall be sent to the Secretary with the title. As early as possible after each meeting, the Secretary shall edit and publish the Proceedings of the Society together with abstracts in a publication authorized by the Society.

3. All applications for membership shall be accompanied by a copy of as many reprints as possible of the published work of the applicant.

THE AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY

Founded December 29, 1913

OFFICERS ELECTED 1942

President—BALDUIN LUCKÉ, University of Pennsylvania Medical School, Philadelphia.

Vice-President—PAUL R. CANNON, University of Chicago, Chicago, Illinois.

Secretary-Treasurer—H. P. SMITH, College of Medicine, State University of Iowa, Iowa City.

Councilors—DOUGLAS H. SPRUNT, Duke University School of Medicine, Durham, N. C., FRIEDA S. ROBSCHEIT-ROBBINS, University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

PAST OFFICERS

1914 R. M. PEARCE, President; JOHN F. ANDERSON, Vice-President; G. H. WHIPPLE, Secretary-Treasurer; HARVEY CUSHING, DAVID MARINE, Councilors. **1915** THEOBALD SMITH, President; G. H. WHIPPLE, Vice-President; PEYTON ROUS, Secretary-Treasurer; DAVID MARINE, R. M. PEARCE, Councilors. **1916** SIMON FLEXNER, President; LEO LOEB, Vice-President; PEYTON ROUS, Secretary-Treasurer; DAVID MARINE, R. M. PEARCE, Councilors. **1917** LUDVIG HEKTOEN, President; LEO LOEB, Vice-President; HOWARD T. KARSNER, Secretary-Treasurer; PAUL A. LEWIS, L. G. ROWNTREE, Councilors. **1918** H. GIDEON WELLS, President; W. G. MACCALLUM, Vice-President; HOWARD T. KARSNER, Secretary-Treasurer; L. G. ROWNTREE, LUDVIG HEKTOEN, Councilors. **1919** W. G. MACCALLUM, President; WILLIAM H. PARK, Vice-President; HOWARD T. KARSNER, Secretary-Treasurer; LUDVIG HEKTOEN, E. L. OPIE, Councilors. **1920** WILLIAM H. PARK, President; F. G. NOVY, Vice-President; HOWARD T. KARSNER, Secretary-Treasurer; E. L. OPIE, WADE H. BROWN, Councilors. **1921** F. G. NOVY, President; HOWARD T. KARSNER, Vice-President; WADE H. BROWN, Secretary-Treasurer; PAUL A. LEWIS, A. R. DOCHEZ, Councilors. **1922** HOWARD T. KARSNER, President EUGENE L. OPIE, Vice-President; WADE H. BROWN, Secretary-Treasurer; A. R. DOCHEZ, GEORGE H. WHIPPLE, Councilors. **1923** EUGENE L. OPIE, President; ALDRED S. WARTHIN, Vice-President; WADE H. BROWN, Secretary-Treasurer; GEORGE H. WHIPPLE, H. GIDEON WELLS, Councilors. **1924** ALDRED S. WARTHIN, President; GEORGE H. WHIPPLE, Vice-President; EDWARD B. KRUMBHAAR, Secretary-Treasurer; H. GIDEON WELLS, FREDERICK L. GATES, Councilors. **1925** GEORGE H. WHIPPLE, President; WADE H. BROWN, Vice-President; EDWARD B. KRUMBHAAR, Secretary-Treasurer; FREDERICK L. GATES, DAVID MARINE, Councilors. **1926** WADE H. BROWN, President; DAVID MARINE, Vice-President; EDWARD B. KRUMBHAAR, Secretary-Treasurer; FREDERICK L. GATES, WILLIAM F. PETERSEN, Councilors. **1927** DAVID MARINE, President; EDWARD B. KRUMBHAAR, Vice-President; CARL V. WELLER, Secretary-Treasurer; WILLIAM F. PETERSEN, FREDERICK L. GATES, Councilors. **1928** EDWARD B. KRUMBHAAR, President; WILLIAM F. PETERSEN, Vice-President; CARL V. WELLER, Secretary-Treasurer; FREDERICK L. GATES, SAMUEL R. HAYTHORN, Councilors. **1929** WILLIAM F. PETERSEN, President; FREDERICK L. GATES, Vice-President; CARL V. WELLER, Secretary-Treasurer; SAMUEL R. HAYTHORN, PEYTON ROUS, Councilors. **1930** FREDERICK L. GATES, President; SAMUEL R. HAYTHORN, Vice-President; C. PHILLIP MILLER, Secretary-Treasurer; PEYTON ROUS, CARL V. WELLER, Councilors. **1931** SAMUEL R. HAYTHORN, President; PEYTON ROUS, Vice-President; C. PHILLIP MILLER, Secretary-Treasurer; CARL V. WELLER, S. BURT WOLBACH, Councilors. **1932** PEYTON ROUS, President; CARL V. WELLER, Vice-President; C. PHILLIP MILLER, Secretary-Treasurer; S. BURT WOLBACH, OSKAR KLOTZ, Councilors. **1933** CARL V. WELLER, President; S. BURT WOLBACH, Vice-President; C. PHILLIP MILLER, Secretary-Treasurer; OSKAR KLOTZ, ALPHONSE R. DOCHEZ, Councilors. **1934** S. BURT WOLBACH, President; OSCAR KLOTZ, Vice-President; SHIELDS WARREN, Secretary-Treasurer; C. PHILLIP MILLER, ALPHONSE R. DOCHEZ, Councilors. **1935** OSKAR KLOTZ, President; ALPHONSE R. DOCHEZ,

Vice President. SHIELDS WARREN, Secretary-Treasurer; MORTON MCCUTCHEON, C. PHILLIP MILLER, Councilors. **1936** ALPHONSE R. DOCHEZ, President; C. PHILLIP MILLER, Vice-President; SHIELDS WARREN, Secretary-Treasurer; MORTON MCCUTCHEON, ERNEST W. GOODPASTURE, Councilors. **1937** C. PHILLIP MILLER, President; MORTON MCCUTCHEON, Vice-President; PAUL R. CANNON, Secretary-Treasurer; ERNEST W. GOODPASTURE, SHIELDS WARREN, Councilors. **1938** MORTON MCCUTCHEON, President; ERNEST W. GOODPASTURE, Vice President; PAUL R. CANNON, Secretary-Treasurer; SHIELDS WARREN, JESSE L. BOLLMAN, Councilors. **1939** ERNEST W. GOODPASTURE, President; SHIELDS WARREN, Vice-President; PAUL R. CANNON, Secretary-Treasurer; JESSE L BOLLMAN, BALDUIN LUCKÉ, Councilors. **1940** SHIELDS WARREN President; JESSE L. BOLLMAN, Vice-President: H. P. SMITH, Secretary-Treasurer; BALDUIN LUCKÉ, PAUL R. CANNON, Councilors. **1941** JESSE L. BOLLMAN, President; BALDUIN LUCKÉ, Vice-President; H P. SMITH, Secretary-Treasurer; PAUL R. CANNON, DOUGLAS H. SPRUNT, Councilors. **1942** BALDUIN LUCKÉ, President; PAUL R. CANNON, Vice-President; H. P. SMITH, Secretary-Treasurer; DOUGLAS H. SPRUNT, FRIEDA S. ROBSCHEIT-ROBBINS, Councilors.

CONSTITUTION

ARTICLE I.—*Name*

The Society shall be named "THE AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY."

ARTICLE II.—*Object*

The object of this Society is to bring the productive investigators in pathology, working essentially by experimental methods, in closer affiliation with the workers in the other fields of experimental medicine.

ARTICLE III.—*Time and Place of Meeting*

The Society shall meet at the same time and place as the Federation of American Societies for Experimental Biology, which comprises at present the American Physiological Society, the American Society of Biological Chemists, the American Society for Pharmacology and Experimental Therapeutics, and the American Society for Experimental Pathology.

ARTICLE IV.—*Membership*

SECTION 1. Any American investigator who, through the use of experimental methods, has, within three years prior to his candidacy, contributed meritorious work in pathology, is eligible to membership.

SEC. 2. It shall be the policy of the Society to restrict its membership to as small numbers as is compatible with the maintenance of an active existence.

SEC. 3. There shall be two classes of members: active and honorary members.

Active members: Candidates for active membership shall be nominated at or before an annual meeting by two members of the Society. The nominators shall present to the Secretary in writing evidence of the candidate's qualifications for membership. Nominations approved by the Council shall be presented to the Society for election at the next annual meeting following nomination. For election a favorable ballot by a majority of the members present is necessary.

Honorary members: These may be elected from the active list or from the group of distinguished investigators at home or abroad who have contributed to the knowledge of pathology by experimental study. They shall be elected only by the unanimous vote of the members present at time of nomination.

SEC. 4. Active members shall pay such annual dues as are determined upon, from year to year, by the Council. Honorary members shall pay no dues, are not eligible to office, and have no vote in the business affairs of the Society, but they shall have all the privileges of the active members in the scientific proceedings.

SEC. 5. Upon failure of an active member to pay dues for two years, notice shall be given to the member by the Secretary. At the end of the third year, if dues are still unpaid, such failure constitutes forfeiture of membership.

SEC. 6. A motion for expulsion of a member must be thoroughly investigated by the Council; at this investigation the accused shall be afforded a hearing or may be represented by a member. Expulsion can be accomplished only after a unanimous vote by the Council in favor of expulsion, sustained by a four-fifths vote of the members present at the meeting.

ARTICLE V.—*Officers*

The management of the Society shall be vested in a Council of five members, consisting of a President, a Vice-President, a Secretary-Treasurer, and two other members who shall be nominated by the Council and elected by the Society. Officers are elected by a majority vote. Vacancies shall be filled by the Council for the unexpired term.

The President and Vice-President shall hold office for one year and are ineligible for re-election during the following year. The Secretary-Treasurer is eligible for re-election. Councilors shall hold office for two years and are elected on alternate years. At the first election one Councilor shall be elected for a short term of one year.

ARTICLE VI.—*Quorum*

SECTION 1. Three constitute a quorum of the Council. The Council decides by a majority vote.

SEC. 2. A quorum of the Society for transaction of business shall be one-fourth of the total membership. In all questions brought before the Society a majority vote of those present shall decide, except as elsewhere provided for.

ARTICLE VII.—*Annual Meeting*

SECTION 1. Papers shall be limited to ten minutes. However, on motion and with unanimous consent, the time may be prolonged by a period not exceeding five minutes. The Council may make provision for longer papers on suitable occasions.

SEC. 2. The subjects of papers must be confined to experimental work in pathology. In doubtful cases a liberal interpretation by the President and Secretary may prevail. The Council may invite, however, presentations dealing with any subject which it considers of considerable interest to the Society.

ARTICLE VIII.—*Change of Constitution*

A motion concerning a change of the Constitution must be presented to the Council in writing by three members, and must be communicated to the members by the Secretary at least four weeks before the annual meeting. At this meeting such a change may be established when accepted by a four-fifths vote of the members present.

BY-LAWS

1. There must be in each year at least one meeting of the Council, which shall take place not later than the evening before the annual meeting.

2. At the end of the first session of the annual meeting the Secretary shall read the report of the Council. This report shall include (1) names of persons recommended for membership, (2) nominations for offices, (3) matters of general interest. The Secretary shall exhibit in a conspicuous place the names of candidates for membership recommended by the Council, together with the evidence of the qualifications of the candidates.

3. The election of officers and of new members, changes in the Constitution, etc., shall be voted upon at the end of the first session.

4. Changes in the By-Laws may be determined by a majority vote of those present.

5. In the year that a new Secretary-Treasurer is elected the incoming Council Member elected that year, or another member of the Council, shall become Assistant Secretary-Treasurer for the duration of the term of the Secretary-Treasurer.

THE AMERICAN INSTITUTE OF NUTRITION

Founded April 11, 1933; Incorporated November 16, 1934
Member of Federation 1940

OFFICERS ELECTED 1943

President—H. B. LEWIS.
Vice-President—ICIE G. MACY-HOOBLER.
Secretary—ARTHUR H. SMITH.
Treasurer—W. H. SEBRELL, JR.
Councilors—LYDIA J. ROBERTS, GENEVIEVE STEARNS and T. H. JUKES.
Nominating Committee—C. G. KING, Chairman, H. J. ALMQUIST, N. B. GUERRANT, HAZEL STIEBELING, H. A. MATTILL.

PAST OFFICERS

1933 L. B. MENDEL, President; H. C. SHERMAN, Vice-President; J. R. MURLIN, Secretary-Treasurer; E. F. DUBOIS, M. S. ROSE, Councilors. **1934** J. R. MURLIN, President; E. F. DUBOIS, Vice-President; ICIE G. MACY, Secretary; W. M. BOOTHBY, Treasurer; A. H. SMITH, AGNES FAY MORGAN, R. M. BETHKE, Councilors. **1935** J. R. MURLIN, President; E. F. DUBOIS, Vice-President; ICIE G. MACY, Secretary; G. R. COWGILL, Treasurer; A. H. SMITH, R. M. BETHKE, L. A. MAYNARD, Councilors. **1936** E. F. DUBOIS, President; MARY SWARTZ ROSE, Vice-President; G. R. COWGILL, Treasurer; ICIE G. MACY, Secretary; R. M. BETHKE, L. A. MAYNARD, C. A. ELVEHJEM, Councilors. **1937** MARY S. ROSE, President; E. V. MCCOLLUM, Vice-President; G. R. COWGILL, Treasurer; ICIE G. MACY, Secretary; L. A. MAYNARD, C. A. ELVEHJEM, P. E. HOWE, Councilors. **1938** E. V. MCCOLLUM, President; T. M. CARPENTER, Vice-President; G. R. COWGILL, Treasurer; L. A. MAYNARD, Secretary; C. A. ELVEHJEM, P. E. HOWE, HELEN S. MITCHELL, Councilors. **1939** H. C. SHERMAN, President; T. M. CARPENTER, Vice-President; G. R. COWGILL, Treasurer; L. A. MAYNARD, Secretary; P. E. HOWE, HELEN S. MITCHELL, A. H. SMITH, Councilors. **1940** THORNE M. CARPENTER, President; A. G. HOGAN, Vice-President; L. A. MAYNARD, Secretary; W. H. SEBRELL, JR., Treasurer; HELEN S. MITCHELL, ARTHUR H. SMITH, LYDIA J. ROBERTS, Councilors. **1941** A. G. HOGAN, President; L. A. MAYNARD, Vice-President; ARTHUR H. SMITH, Secretary; W. H. SEBRELL, JR., Treasurer; T. H. JUKES,

LYDIA J. ROBERTS, H. B. LEWIS, Councilors.
1942 L. A. MAYNARD, President; H. B. LEWIS, Vice-President; ARTHUR H. SMITH, Secretary; W. H. SEBRELL, JR., Treasurer; LYDIA J. ROBERTS, GENEVIEVE STEARNS, T. H. JUKES, Councilors.

CONSTITUTION

1. The name of the proposed society is the "AMERICAN INSTITUTE OF NUTRITION."

2. The purposes of the society are to further the extension of the knowledge of nutrition and to facilitate personal contact between investigators in nutrition and closely related fields of interest.

3. The management of the American Institute of Nutrition shall be vested in a council consisting of the President, Vice-President, Secretary, Treasurer and three additional members.

BY-LAWS

ARTICLE I—*Membership*

SECTION 1. There shall be two classes of members, members and emeritus members. The number of members shall be limited to 300 exclusive of emeritus members.

SEC. 2. *Eligibility for membership:* Members. Qualified investigators who have independently conducted and published meritorious original investigations in some phase of the chemistry or physiology of nutrition and who have shown a professional interest in nutrition for at least 5 years shall be eligible for membership in the Society. Emeritus Members. Members in good standing who have reached the age of 65 years shall become emeritus members. A member in good standing and for sufficient reason may by vote of the Council be made an emeritus member. Emeritus members shall be entitled to vote but not hold office.

SEC. 3. *Nomination:* Nominations for membership shall be made and seconded by members of the Society on blanks furnished by the Secretary. Nominations shall be submitted to the Council who shall determine eligibility and make recommendation to the Society at a regular meeting.

SEC. 4. *Election to membership:* A. A nominee for membership may be voted for by ballot at any meeting of the Society after the Council has reported its findings on his eligibility. B. A majority of the ballots cast shall elect.

SEC. 5. *Forfeiture:* If a majority of the Council after due notice to the member in question and opportunity for a hearing, shall decide that the interests of the Society require the expulsion of a member, the Secretary shall send a notice of this decision to each member at least two weeks before the next annual meeting. At this meeting the Secretary shall, on behalf of the Council, propose the expulsion; and if two-thirds of the members present vote for it, the member shall be expelled, his assessment for the current year shall be returned to him, and he shall cease to be a member of the Society.

ARTICLE II—*Meetings and Quorum*

SECTION 1. *Annual:* The annual meeting of the Society shall be held on the date fixed by the Certificate of Incorporation.

SEC. 2. *Special:* A special meeting may be called at any time by the President, or in case of his absence or disability, by the Vice-President, and must be called at the request in writing of a majority of the Council or fifty members of the Society. Notice specifying the purpose of such meeting shall be mailed to each member at least ten days previous thereto. The Council shall select the places at which meetings shall be held.

SEC. 3. *Quorum:* Thirty members shall constitute a quorum at all meetings of the Society, but in the absence of a quorum any number shall be sufficient to adjourn to a fixed date.

ARTICLE III—*Officials*

SECTION 1. *Officers:* The officers shall be a President, and a Vice-President, who shall be elected annually, and a Secretary and Treasurer, each of whom shall be elected to serve for a term of three years. These officers shall be elected by the members of the Society. Their terms of office shall commence on May 1 of the year in which they are elected.

SEC. 2. *Council:* The officers so selected and three additional members, one of whom shall be elected at each annual meeting to serve a term of three years, shall constitute a Board of Trustees and shall be known as 'The Council.' (When this provision is first put into effect one member shall be elected for 1 year, one for 2 years and the third for 3 years.)

SEC. 3. *Duties of Officers:* The powers and duties of the officers elected by the Society shall be such as usually devolve upon their respective positions.

ARTICLE IV—*The Council*

SECTION 1. *Powers:* The general management of the Society during the intervals between meetings shall be vested in the Council, which shall regularly perform the ordinary duties of an executive committee and possess all the powers conferred upon the Board of Trustees of an educational institution chartered by the Education Department of the University of the State of New York. A permanent charter was issued to the American Institute of Nutrition under date of November 16, 1934.

SEC. 2. *Reports:* The Council shall report to the Society its findings on the eligibility of candidates

for membership, and on all charges of a violation of these By-Laws.

ARTICLE V—*Nominating Committee*

SECTION 1. *Membership:* A. The Nominating Committee shall consist of five members appointed for the coming year by the retiring President. Members who have served on the Nominating Committee for two consecutive years shall be ineligible for reappointment until after a lapse of one year. B. The President shall designate one member to be Chairman of the Nominating Committee.

SEC. 2. *Nomination of Officials:* A. The Nominating Committee shall make at least one nomination for each of the four offices, for each of the additional positions on the Council to be filled by vote of the members and for each of the positions on the Editorial Board to be vacated at the time of the annual meeting. Any member of the Institute may submit nominations to the Nominating Committee for its consideration along with those nominations made by the members of the Nominating Committee. B. The nominations by the Nominating Committee shall be transmitted to the Secretary at least six weeks before the annual meeting at which they are to be considered. C. The Secretary shall send to every member, at least two weeks before the annual meeting, a printed ballot containing the list of nominees and space for such additional names as the member wishes to propose, and at the same time shall notify the members that they may vote by mail, returning to the Secretary the marked ballot in the envelope provided, at such a time and place as the Secretary may designate, or the ballot may be delivered to the Secretary at the beginning of the business session at which the elections are to take place.

SEC. 3. *Election of Officials:* A. At the beginning of the business session the Secretary shall present to the tellers, appointed by the President, the ballots submitted by the members and the ballots shall be counted forthwith. B. A majority of votes cast shall be necessary to elect an official.

SEC. 4. *Filling of Vacancies:* A. The Nominating Committee shall fill all vacancies in elective positions except such as may occur at a meeting of the Society. B. The President of the Society shall fill all vacancies in appointive positions.

ARTICLE VI—*Financial*

SECTION 1. *Dues:* The dues shall be the annual cost of subscription to The Journal of Nutrition for members plus an annual assessment which shall be determined by majority vote at the annual meetings, upon recommendation of the Council, and shall be due within a month after the annual meeting. Emeritus members are not required to subscribe to The Journal of Nutrition nor to pay assessments other than those levied on all members of the Federation by its Executive Committee.

SEC. 2. *Expenditures:* No expenditures from the general funds of the Society except those required in the performance of the ordinary official duties shall be made except by vote of the Society or the Council.

SEC. 3. *Penalty for non-payment of dues:* A. Members in arrears for dues for two consecutive years shall forfeit their membersip. B. Delinquent members may be reinstated by the Council provided all indebtedness to the Society is liquidated.

ARTICLE VII—*The Journal of Nutrition*

SECTION 1. The American Institute of Nutrition designates The Journal of Nutrition as its official organ of publication.

SEC. 2. In accordance with the expressed wish of the Wistar Institute of Anatomy and Biology, owner and publisher of The Journal of Nutrition, the American Institute of Nutrition shall nominate members of the Editorial Board for its official organ. A. The editorial management of The Journal of Nutrition shall be vested in an Editorial Board consisting of an Editor and twelve Board Members. B. The Editor shall be chosen by the Editorial Board to serve a term of five years beginning May 1 of the year in which he is chosen, and shall be eligible for reëlection. The Editor shall have the power to designate one of the Board Members to serve as his assistant, and such an appointee shall be called Associate Editor. C. Three members of the Institute shall be nominated by the Nominating Committee for membership on the Editorial Board each year to serve a term of four years, replacing three retiring members and taking office May 1 of the year in which they are elected. In the event of a vacancy in the membership of the Editorial Board occurring through death or other reason, the Nominating Committee, for each such vacancy to be filled shall make an additional nomination. In this event the nominees elected who receive the greatest number of votes shall serve the longest term of vacancies to be filled. D. Retiring members of the Editorial Board shall not be eligible for renomination until one year after their retirement.

ARTICLE VIII—*Papers on Scientific Subjects*

SECTION 1. The Secretary shall be authorized to arrange programs for the scientific sessions at the annual meetings.

ARTICLE IX—*Changes in Constitution and By-Laws*

SECTION 1. Proposed changes in the Constitution and By-Laws must be sent in writing to the Secre-

tary at least one month before the date of the meeting at which they are to be considered, and must be signed by at least three members. The Secretary shall send a printed copy of any proposed change to each member at least two weeks before the next meeting and shall notify all members that they may vote by proxy.

SEC. 2. If at this meeting two-thirds of the votes cast shall favor the proposed change, it shall be made.

THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS

Founded June 19, 1913; Member of Federation 1942

OFFICERS ELECTED 1942

President—JACQUES J. BRONFENBRENNER, Washington University School of Medicine, St. Louis, Mo.

Secretary-Treasurer—ARTHUR F. COCA, Pearl River, N. Y.

Council—JACQUES J. BRONFENBRENNER, ARTHUR F. COCA, MICHAEL HEIDELBERGER, 620 W. 168 St., New York City, PAUL R. CANNON, University of Chicago, Chicago, Ill., KARL F. MEYER, Medical Center, San Francisco, Cal., GEORGE P. BERRY, University of Rochester, Rochester, N. Y., DONALD T. FRASER, Connaught Laboratories, University of Toronto, Toronto, Canada, SANFORD B. HOOKER, (Ex officio), 80 East Concord St., Boston, Mass., JOHN F. ENDERS, (Ex officio), Harvard University School of Medicine, Boston, Mass.

PAST OFFICERS

Presidents—1913 GERALD B. WEBB. 1915 JAMES W. JOBLING. 1916 RICHARD WEIL. 1917 JOHN A. KOLMER. 1918 WILLIAM H. PARK. 1919 HANS ZINSSER. 1920 RUFUS I. COLE. 1921 FREDERICK P. GAY. 1922 GEORGE W. MCCOY. 1923 H. GIDEON WELLS. 1924 FREDERICK G. NOVY. 1925 WILFRED H. MANWARING. 1926 LUDVIG HEKTOEN. 1927 KARL LANDSTEINER. 1928 EUGENE L. OPIE. 1929 OSWALD T. AVERY. 1930 STANHOPE BAYNE-JONES. 1931 ALPHONSE R. DOCHEZ. 1932 AUGUSTUS B. WADSWORTH. 1933 THOMAS M. RIVERS. 1934 FRANCIS G. BLAKE. 1935 WARFIELD T. LONGCOPE. 1936 SANFORD B. HOOKER. 1937 CARL TENBROECK. 1938 DONALD T. FRASER. 1939 GEORGE P. BERRY. 1940 PAUL R. CANNON. 1941 KARL F. MEYER. 1942 JACQUES J. BRONFENBRENNER.

Vice-Presidents—1913-1915 GEORGE W. ROSS. 1915 GEORGE P. SANBORN. 1916 JOHN A. KOLMER.

Secretary—1913-1918 MARTIN J. SYNNOTT.

Treasurer—1913-1918 WILLARD J. STONE.

Secretary-Treasurer—1918-*date*. ARTHUR F. COCA.

CONSTITUTION AND BY-LAWS

Adopted April 6, 1917

ARTICLE I

SECTION 1. This Association shall be called "The American Association of Immunologists."

SEC. 2. The purpose of the Association shall be to study the problems of immunology and its application to clinical medicine.

ARTICLE II

SECTION 1. The Association shall be governed by a Council of seven, which shall consist of the officers of the association and enough active members to make a total of seven members.

SEC. 2. The officers of the Association shall be a President, a Secretary, and a Treasurer, who shall be nominated annually by the Council, and elected by the Society to serve for one year. Nominations of officers may be made also by members of the Society.

SEC. 3. No councilor is eligible for re-election until after one year, except the Secretary and the Treasurer, who are eligible for re-election.

SEC. 4. If any councilor without good and sufficient reason fails to attend two consecutive meetings of the Council he shall be considered to have resigned.

SEC. 5. The same person shall not serve as President more than one year consecutively.

SEC. 6. It is the duty of the Council to conduct the business of the Association and to elect the new members. Should a vacancy occur in the Council otherwise than by the expiration of the term of service, the Council may elect a member to serve for the unexpired portion of the term.

ARTICLE III

SECTION 1. Active Members. Any one actively engaged in the systematic study of problems relating to immunology shall be eligible to active membership.

ARTICLE IV

Candidates for membership shall be nominated by two active members of the Association who shall present in writing to the Council evidence of the fitness of the candidates to become members of the Association.

ARTICLE V

If a majority of the Council shall decide that the interests of the Society require the expulsion of a member, the Secretary shall send a notice of this decision to each active member at least two weeks before the next annual meeting. At this meeting the Secretary shall, on behalf of the Council, propose the expulsion; and if two-thirds of the members present vote for it, the member shall be expelled, his assessment for the current year shall be returned to him, and he shall cease to be a member of the Society.

ARTICLE VI

SECTION 1. A quorum of the Council for the transaction of all business shall be three.

SEC. 2. Any number of members present at the time appointed for the annual meeting of the Association, shall constitute a quorum.

BY-LAWS

1. A regular meeting of the Association shall be held annually at such time and place as the Council shall determine.

2. Special meetings of the Association may be held at the discretion of the Council.

3. These regular and special meetings shall be open to all members of the Association.

4. A meeting of the Council shall be held shortly before each annual session of the Association.

5. Hereafter each Councilor shall serve for a period of six years. Under this rule the service of one member and also that of the Secretary-Treasurer terminates at the meeting of 1936. At that meeting two members shall be elected to the Council, one of whom may serve as Secretary-Treasurer. Thereafter the period of service of these two members shall run concurrently; hence, two members must be elected to the Council every six years in order to maintain a membership of seven.

6. Past Presidents are honorary members of the Council.

7. The titles of all communications to be presented before the Association shall be approved by the Council.

8. Failure of an active member to offer a paper at least once in three years shall be equivalent to resignation. If in its judgment there is sufficient reason the Council may, in individual cases, suspend this rule.

9. The dues of the Association shall be fixed annually by the Council.

10. Failure to pay dues for three successive years shall constitute annulment of membership.

11. The constitution and by-laws may be amended by a two-thirds vote of the active members present at any regular meeting.

12. No amendment shall be adopted at the meeting at which it is proposed.

13. The Journal of Immunology, which is the property and official organ of this Association, shall be administered for the Association by an editorial staff to consist of an Editor-in-Chief and at least three Associate Editors, with the advice of a Board of Editors.

14. The members of the editorial staff shall be elected or may be removed by a majority vote of the Council of the Association.

ALPHABETICAL LIST OF ALL MEMBERS OF THE SIX SOCIETIES

The parenthesis following each listed name gives the Society affiliation and year of election:

(1) The American Physiological Society*
(2) The American Society of Biological Chemists
(3) The American Society for Pharmacology and Experimental Therapeutics
(4) The American Society for Experimental Pathology
(5) The American Institute of Nutrition
(6) The American Association of Immunologists

HONORARY MEMBERS

Castaneda, M. Ruiz, M.D. Investigaciones Medicas, Hospital General, Mexico, D. F. *Director, Department of Medical Research.* (6, 1942)

Chopra, R. N., M.A., M.D., Sc.D.(Cantab), F.R.C.P. (London) P.I.E. School of Tropical Medicine, Calcutta, India. *Director; Professor of Pharmacology.* (3, 1938)

Dale, H. H. Medical Research Council, National Institute for Medical Research, Hampstead, London, N.W. 3, England. *Director, National Institute for Medical Research.* (3, 1926)

Flexner, Simon, M.D., Sc.D.(hon.), LL.D. 520 E. 86th St., New York City. *Emeritus Director, Rockefeller Institute for Medical Research.* (6, 1920)

Hektoen, Ludvig, M.D. 629 S. Wood St., Chicago, Ill. *President, Chicago Tumor Institute.* (6, 1919)

Hitchens, Arthur P., M.D. Medical School, University of Pennsylvania, Philadelphia. *Professor of Public Health and Preventive Medicine; Lt. Col., M.C., U.S.A.* (6, 1913)

Houssay, Bernardo A., M.D. Facultad de Medicina, Universidad de Buenos Aires, Instituto de Fisiologia, Buenos Aires, Argentina. *Professor of Physiology and Director.* (1, 1942)

Huntoon, F. M., M.D. Woodbridge, Conn. (6, 1918)

Koller, Carl, M.D. 30 W. 58th St., New York City. (3, 1930)

Lowei, Otto, M.D. New York University College of Medicine, 477 First Ave., New York City. *Research Professor in Pharmacology.* (3, 1941)

McCoy, George Walter, M.D. Louisiana State University Medical School, New Orleans. *Director, Department of Public Health.* (6, 1916)

Novy, Frederick G., M.D., Sc.D., LL.D. 721 Forest Ave., Ann Arbor, Mich. *Dean Emeritus and Professor Emeritus of Bacteriology, Medical School, University of Michigan.* (6, 1920)

Rosenau, Milton J., M.D., A.M. Medical School, University of North Carolina, Chapel Hill. *Director, School of Public Health; Professor of Epidemiology, School of Public Health.* (6, 1918)

Sherrington, Sir Charles S., O.M., Sc.D., M.D., F.R.S. "Broomside," Valley Road, Ipswich, England. *Former Wayneflete Professor of Physiology, Oxford University; Former President of the Royal Society.* (1, 1904)

Sordelli, A. Institute of Bacteriology, Department of Public Health, Buenos Aires, Argentina. *Director.* (6, 1942)

Straub, Walther, M.D. University of Munich, Germany. (3, 1927)

MEMBERS

Abramson, David Irwin, M.D. O'Reilly General Hospital, Springfield, Mass. *Captain, Medical Corps.* (1, 1937)

Abramson, Harold A., M.D. 133 E. 58th St., New York City. *Assistant Professor of Physiology, College of Physicians and Surgeons, Columbia University.* (1, 1930; 2, 1934)

Abreu, Benedict E., M.S., Ph.D. University of Georgia School of Medicine, Augusta. *Associate Professor of Pharmacology.* (3, 1941)

Acheson, George H., M.D. Harvard Medical School, 25 Shattuck St., Boston, Mass. *Instructor in Physiology.* (1, 1942)

Adams, Mildred, M.A., Ph.D. Takamine Laboratory, Clifton, N. J. *Research Chemist.* (2, 1934)

Adams, R. Charles, M.D., C.M., M.S. (Anesthesiology), Mayo Clinic, Rochester, Minn. *Instructor in Anesthesia, Mayo Foundation, University of Minnesota. Member of Mayo Clinic Staff, Section on Anesthesia.* (3, 1942)

Adams, W. Lloyd, M.A., Ph.D. Albany Medical College, Albany, N. Y. *Assistant Professor of Physiology and Pharmacology.* (3, 1942)

Addis, Thomas, M.D., M.R.C.P. Lane Hospital, San Francisco, Calif. *Professor of Medicine, Stanford University.* (1, 1922)

Addison, William H. F., M.D. School of Medicine, University of Pennsylvania, Philadelphia. *Professor of Histology and Embryology.* (1, 1928)

* Recommended by the Council of the American Physiological Society for election at the next annual meeting of the Society.

Adler, Harry F., M.S., Ph.D.* Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Instructor in Physiology.* (1, 1943)

Adolph, Edward Frederick, Ph.D. School of Medicine and Dentistry, University of Rochester, Rochester, N. Y. *Associate Professor of Physiology.* (1, 1921)

Adolph, William Henry, Ph.D. Yenching University, Peiping, China. *Professor of Biochemistry.* (5, 1934)

Albritton, Errett C., M.D. George Washington University Medical School, 1339 H St., N.W., Washington, D. C. *Professor of Physiology and Head of the Department of Physiology.* (1, 1933)

Allen, Charles Robert, Ph.D.* University of Texas, School of Medicine, Galveston. *Assistant Professor of Department of Anesthesiology.* (1, 1943)

Allen, Frank N., M.D. Lahey Clinic, 605 Commonwealth Ave., Boston, Mass. *Co-director of the Medical Department.* (4, 1930)

Allen, Frederick M., M.D. 1031 Fifth Ave., New York City. *Professor of Medicine, Polyclinic Medical School and Hospital.* (1, 1924; 4, prior to 1920)

Allen, J. Garrott, M.D.* University of Chicago, University Clinics, Chicago, Ill. *Instructor in Surgery.* (1, 1943)

Allen, Lane, M.S., Ph.D., M.D. University of Georgia School of Medicine, University Place, Augusta. *Associate Professor of Anatomy.* (1, 1939)

Allen, Willard M., M.D. Washington University School of Medicine, 630 S. Kingshighway Blvd., St. Louis, Mo. *Professor of Obstetrics and Gynecology.* (1, 1934)

Allen, William F., Ph.D. University of Oregon Medical School, Portland. *Professor of Anatomy.* (1, 1929)

Alles, Gordon A., M.S., Ph.D. 770 S. Arroyo Parkway, Pasadena, Calif. *Lecturer in Pharmacology, University of California Medical School, San Francisco, and Research Associate in Biology, California Institute of Technology, Pasadena.* (1, 1932; 3, 1941)

Almquist, Herman J., Ph.D. University of California, Division of Poultry Husbandry, Berkeley. *Associate Professor of Poultry Husbandry.* (2, 1937; 5, 1937)

Alvarez, Walter C., M.D. Mayo Clinic, Rochester, Minn. *Professor of Medicine, Mayo Foundation.* (1, 1917; 3, 1921)

Alving, Alf Sven, M.D. Billings Hospital, University of Chicago, 950 E. 59th St., Chicago, Ill. *Associate Professor of Medicine.* (1, 1939)

Amberg, Samuel, M.D., F.A.A.P. Mayo Clinic, Rochester, Minn. *Associate in Pediatrics, Mayo Clinic; Associate Professor of Pediatrics, Mayo Foundation* (1, 1903; 2, 1906; 3, 1909)

Amberson, William R., Ph.D. University of Maryland School of Medicine, Baltimore. *Professor of Physiology.* (1, 1924)

Ambrose, Anthony M., M.S., Ph.D. Department of Pharmacology, Stanford University School of Medicine, San Francisco, Calif. *Associate Pharmacologist, U. S. Department of Agriculture, Bureau of Agricultural Chemistry and Engineering.* (3, 1937)

Amoss, Harold L., M.D., M.S., D.P.H., Sc.D. 21 Field Point Road, Greenwich, Conn. (4, 1922; 6, 1917)

Andersch, Marie A., Ph.D. University Hospital, Baltimore, Md. *Biochemist, University Hospital, Instructor in Medicine, University of Maryland.* (2, 1940)

Andersen, Dorothy H., M.D. Babies Hospital, Broadway and 167th St., New York City. *Associate in Pathology, Columbia University.* (4, 1935)

Anderson, Evelyn M., M.A., M.D. University of California Hospital, San Francisco. *Assistant Professor of Medicine.* (1, 1934)

Anderson, Hamilton H., M.S., M.D. 1405 Drake Ave., Burlingame, Calif. *Professor of Pharmacology, Peiping Union Medical College.* (3, 1931)

Anderson, Oscar Daniel, Ph.D. Stimson Hall, Cornell University, Ithaca, N. Y. *Assistant Professor of Physiology.* (1, 1939)

Anderson, Rudolph J., Ph.D. Sterling Laboratory, Yale University, New Haven, Conn. *Professor of Chemistry.* (2, 1915)

Anderson, W. A. D., M.A., M.D. St. Louis University School of Medicine, St. Louis, Mo. *Assistant Professor of Pathology.* (4, 1941)

Anderson, William E., M.A. Eastern State Farmers' Exchange, Westbrook Farm, Rockville, Conn. *Biochemist.* (2, 1931; 5, 1933)

Andervont, H. B., Sc.D. National Cancer Institute, Bethesda, Md. *Principal Biologist, U. S. Public Health Service.* (4, 1939)

Andrews, James C., Ph.D. University of North Carolina, Chapel Hill. *Professor of Biological Chemistry.* (2, 1925)

Andrus, E. Cowles, M.D. Johns Hopkins Hospital, Baltimore, Md. *Assistant Visiting Physician; Associate Professor of Medicine, Johns Hopkins University.* (1, 1925)

Angerer, Clifford, Ph.D.* Ohio State University, Columbus. *Instructor in Physiology.* (1, 1943)

Angevine, D. Murray, M.D. Alfred I. du Pont Institute, Wilmington, Del. *Pathologist; Visiting Assistant Professor of Pathology, University of Pennsylvania.* (4, 1940)

Angier, Roswell Parker, Ph.D. % Los Rauchos Perkins, Tucson, Ariz. *Professor of Psychology, Yale University.* (1, 1906)

Ansbacher, Stefan, M.S., D.Sc. Research Laboratory, International Vitamin Corporation, 84–48 129th St., Richmond Hill, L. I., N. Y. *Scientific Director.* (2, 1939)

Anson, Mortimer L., Ph.D. Continental Foods, Hoboken, N. J. *Director of Biochemical Research.* (2, 1937)

Apperly, Frank L., M.A., D.Sc., M.D., F.R.C.P. Medical College of Virginia, Richmond. *Professor of Pathology.* (4, 1936)

Arkin, Aaron, M.A., M.D., Ph.D. Suite 2006, 25 E. Washington St., Chicago, Ill. *Associate Professor of Medicine, Rush Medical College, Univ. of Chicago; Professor and Chairman, Dept. of Medicine, Cook County Graduate School.* (1, 1914; 3, 1919)

Armstrong, W. D., M.S., M.D., Ph.D. Medical Sciences Bldg., University of Minnesota, Minneapolis. *Associate Professor of Physiological Chemistry.* (2, 1938)

Arnold, Lloyd, A.M., M.D. 1538 E. 57th St., Chicago, Ill. (4, 1930; 6, 1925)

Arnow, L. Earle, Ph.D., M.D. Medical Research Division, Sharp and Dohme, Glenolden, Pa. *Director of Biochemical Research.* (2, 1940)

Aronson, Joseph D., M.D. Hospital, Fort Belvoir, Va. *Associate Professor of Bacteriology, Phipps Institute, University of Pennsylvania; Major, M. C., U. S. A.* (4, 1927; 6, 1925)

Ascham, Leah, Ph.D. Kansas State College, Manhattan. *Associate Professor, School of Home Economics.* (5, 1935)

Ashby, Winifred M., Ph.D. 305 10th St., N.E., Washington, D. C. *Senior Scientist, Federal Security Agency (St. Elizabeth's Hospital).* (6, 1923)

Ashman, Richard, M.S., Ph.D. School of Medicine, Louisiana State University, New Orleans. *Professor of Physiology.* (1, 1925)

Astwood, Edwin Bennet, M.D., C.M., Ph.D. Harvard Medical School, 25 Shattuck St., Boston, Mass. *Assistant Professor of Pharmacotherapy.* (1, 1939)

Aub, Joseph C., M.D. Collis P. Huntington Memorial Hospital, 695 Huntington Ave., Boston, Mass. *Associate Professor of Medicine, Harvard Medical School.* (1, 1919; 5, 1933)

Auer, John, M.D. 1402 S. Grand Blvd., St. Louis, Mo. *Professor of Pharmacology and Director of the Department, St. Louis University School of Medicine.* (1, 1905; 3, 1908)

Austin, J. Harold, M.D. 711 Maloney Clinic, 36th and Spruce Sts., Philadelphia, Pa. *Director, Pepper Laboratory.* (2, 1922)

Austin, Richard Sisson, M.D. Cincinnati General Hospital, University of Cincinnati, Cincinnati, O. *Professor of Pathology.* (4, 1927)

Avery, O. T., M.D., Sc.D., LL.D. Hospital of the Rockefeller Institute, 66th St. and York Ave., New York City. *Member Emeritus, Rockefeller Institute for Medical Research.* (4, 1921; 6, 1920)

Axtmayer, Joseph H., A.M., Ph.D. School of Tropical Medicine, San Juan, Porto Rico. *Associate Professor of Chemistry.* (5, 1935)

Babkin, B. P., M.D., D.Sc., F.R.S.C. McGill University, Montreal, Canada. *Professor of Physiology.* (1, 1924)

Bachem, Albert, Ph.D. College of Medicine, University of Illinois, 1853 W. Polk St., Chicago. *Professor of Biophysics.* (1, 1933)

Bachman, Carl, M.D. Mobile Hospital No. 51, c/o Fleet P. O., San Francisco, Calif. *Lieut. Commander.* (2, 1941)

Bachmann, George, M.S., M.D., F.A.C.P. 1088 Lullwater Road, Atlanta, Ga. *Professor of Physiology, Emory University School of Medicine.* (1, 1912)

Baer, Erich, Ph.D. Banting Institute, 100 College St., Toronto, Canada. *Assistant Research Professor of Organic Chemistry, University of Toronto.* (2, 1942)

Baernstein, Harry D., M.S., Ph.D. National Institute of Health, Bethesda, Md. *Biochemist.* (2, 1934)

Baetjer, Anna M., D.Sc. Johns Hopkins School of Hygiene and Public Health, 615 N. Wolfe St., Baltimore, Md. *Associate in Physiology.* (1, 1929)

Bahrs, Alice M., M.A., Ph.D. The Martha Washington Hotel, 10th and Montgomery Sts., Portland, Ore. (1, 1933)

Bailey, Cameron Vernon, M.D., C.M. 303 E. 20th St., New York City. *Clinical Professor of Medicine, New York Post-Graduate Medical School, Columbia University.* (2, 1920; 5, 1933)

Bailey, Orville T., M.D. Harvard University Medical School, 25 Shattuck St., Boston, Mass. *Associate in Pathology; Associate Pathologist, Peter Bent Brigham Hospital.* (4, 1939)

Bailey, Percival, M.D., Ph.D. University of Illinois College of Medicine, 912 S. Wood St., Chicago. *Professor of Neurology and Neurosurgery.* (1, 1941)

Baitsell, George Alfred, A.M., Ph.D. Yale Station, New Haven, Conn. *Professor of Biology, Yale University.* (1, 1915)

Baker, A. B., M.D. University of Minnesota Medical School, 126 Millard Hall, Minneapolis. *Associate Professor of Neuropsychiatry and Neuropathology.* (4, 1940)

Baker, Roger D., M.D. Duke Hospital, Durham, N. C. *Associate Professor of Pathology, Duke University Medical School; Associate Pathologist, Duke Hospital.* (4, 1939)

Baldes, Edward J., A.M., Ph.D. Mayo Foundation, Rochester, Minn. *Assistant Professor of*

Physics, Mayo Foundation, Graduate School, University of Minnesota. (1, 1930)

Baldwin, Francis Marsh, A.M., Ph.D. University of Southern California, Los Angeles. *Professor of Zoology and Director of Experimental Marine Biology.* (1, 1919)

Bale, William F., Ph.D.* University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. *Associate in Radiology.* (1, 1943)

Ball, Eric G., M.A., Ph.D. Harvard Medical School, Boston, Mass. *Associate Professor of Biochemistry.* (2, 1934)

Ball, Howard A., M.D. San Diego County General Hospital, N. Front St., San Diego, Calif. *Pathologist, San Diego County General and Paradise Valley Hospitals.* (4, 1937)

Balls, Arnold Kent, Ph.D. Enzyme Research Laboratory, U. S. Bureau of Agricultural and Industrial Chemistry, Western Regional Research Laboratory, 800 Buchanan St., Albany 6, Calif. *Head Chemist; Adjunct Professor, The George Washington University* (on leave). (2, 1932)

Banus, Mario Garcia, M.Sc., D.Sc. Tufts College Medical School, Boston, Mass. *Associate Professor of Physiology.* (1, 1927)

Bard, Philip, A.M., Ph.D. Johns Hopkins University School of Medicine, 710 N. Washington St., Baltimore, Md. *Professor of Physiology.* (1, 1929)

Barkan, Georg, M.D., Dr. habil. 80 E. Concord St., Boston, Mass. *Former Professor of Pharmacology and Director of the Pharmacological Institute, Univ. of Dorpat (Estonia); Assistant Professor of Biochemistry, Boston University School of Medicine.* (3, 1939)

Barker, S. B., Ph.D. University of Tennessee, Memphis. *Instructor in Physiology.* (1, 1938)

Barlow, Orpheus W., M.D., Ph.D. Winthrop Chemical Co., 33 Riverside Ave., Rensselaer, N. Y. *Director of Biologic and Research Laboratories.* (1, 1936)

Barnes, B. O., A.M., Ph.D. 2220 S. St. Paul, Denver, Colo. *Professor of Health Education, University of Denver.* (1, 1932)

Barnes, LaVerne A., M.S., Ph.D. 7 Maple Ave., Bethesda, Md. *Lieutenant, H-V(S), U.S.N.R. (Epidemiology and Sanitation Unit, National Naval Medical School).* (6, 1931)

Barnes, Richard Henry, Ph.D. Department of Physiology, University of Minnesota, Minneapolis. *Assistant Professor of Physiological Chemistry.* (2, 1941)

Barnes, Thomas C., D.Sc. Hahnemann Medical College, Philadelphia, Penna. *Associate Professor of Physiology.* (1, 1942)

Barott, Herbert G., E.E. U. S. Department of Agriculture, National Agricultural Research Center, Beltsville, Md. *Biophysicist, Animal Nutrition Division, Bureau of Animal Industry.* (5, 1938)

Barrera, S. Eugene, M.D. Psychiatric Institute and Hospital, Columbia University, 722 W. 168th St., New York City. *Principal Research Psychiatrist and Assistant Professor of Psychiatry.* (1, 1937)

Barron, Donald H., M.S., Ph.D., M.A. (Cambridge)* Yale University School of Medicine, New Haven, Conn. *Associate Professor of Physiology.* (1, 1943)

Barron, E. S. Guzman, M.D. Department of Medicine, University of Chicago, Chicago, Ill. *Assistant Professor of Biochemistry.* (2, 1931)

Bartley, S. Howard, Ph.D. Dartmouth Eye Institute, Dartmouth College, Hanover, N. H. *Assistant Professor of Research in Physiological optics.* (1, 1935)

Batchelder, Esther L., A.M., Ph.D. Rhode Island State College, School of Agriculture and Home Economics, Kingston. *Head of Department of Home Economics.* (5, 1933)

Bates, Robert W., Ph.D. Difco Laboratories, Inc., 920 Henry St., Detroit, Mich. *Biochemist.* (2, 1936)

Batterman, Robert C., M.D. New York University College of Medicine, 477 First Ave., New York City. *Instructor in Therapeutics.* (3, 1941)

Baudisch, Oskar, Ph.D. Saratoga Springs, N. Y. *Director of Research, Saratoga Springs Authority, State of New York.* (2, 1931)

Bauer, Johannes H., M.D. Rockefeller Foundation, 49 W. 49th St., New York City. *Member of Staff, International Health Division of the Rockefeller Foundation.* (4, 1935)

Bauer, Walter, M.D. Massachusetts General Hospital, Boston. *Associate Professor and Tutor in Medicine, Harvard Medical School.* (1, 1929)

Bauman, Louis, M.D. Presbyterian Hospital, New York City. *Assistant Professor of Clinical Medicine, Columbia University.* (2, 1912)

Baumann, Carl A., M.S., Ph.D. Biochemistry Building, University of Wisconsin, Madison 8. *Associate Professor of Biochemistry.* (2, 1938; 5, 1938)

Baumann, Emil J., Ph.D. 7 Church Lane, Scarsdale, N. Y. *Chemist, Montefiore Hospital.* (2, 1922)

Baumberger, J. Percy, M.S., Sc.D. Stanford University, Calif. *Professor of Physiology.* (1, 1921)

Bayne-Jones, Stanhope, M.D. Yale University, School of Medicine, New Haven, Conn. *Professor of Bacteriology.* (4, 1927; 6, 1917)

Bazett, Henry C., M.A., M.D., F.R.C.S. University of Pennsylvania, School of Medicine, Philadelphia. *Professor of Physiology.* (1, 1921)

Beach, Eliot F., Ph.D. 660 Frederick St., Detroit, Mich. *Research Associate, Children's Fund of*

Michigan Research Laboratory. (2, 1941; 5, 1942)

Bean, John W., M.S., Ph.D., M.D. University of Michigan, Ann Arbor. *Associate Professor of Physiology.* (1, 1932)

Beard, Howard H., M.A., Ph.D. 1542 Tulane Ave., New Orleans, La. *Professor of Biochemistry, Louisiana State University Medical Center.* (2, 1928; 5, 1933)

Beard, Joseph W., M.D. Duke Hospital, Durham, N. C. *Associate Professor of Surgery.* (4, 1938; 6, 1940)

Beazell, James Myler, Ph.D., M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Instructor in Physiology and Pharmacology.* (1, 1939)

Beck, Claude S., M.D. Lakeside Hospital, Cleveland, O. *Professor of Neurosurgery, Western Reserve University; Associate Surgeon, Lakeside Hospital.* (4, 1930)

Beck, Lyle V., M.S., Ph.D. Hahnemann Medical College, 235 N. 15th St., Philadelphia, Pa. *Instructor in Physiology.* (1, 1941)

Becker, Ernestine, M.A. Johns Hopkins University, Baltimore, Md. *Associate in Biochemistry.* (5, 1938)

Becker, R. Frederick, M.S., Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Instructor in Anatomy.* (1, 1941)

Beckman, Harry, M.D. Marquette University School of Medicine, Milwaukee, Wis. *Professor and Director of the Department of Pharmacology.* (3, 1937)

Beecher, Henry K., M.D. Massachusetts General Hospital, Boston. *Dorr Professor of Research in Anaesthesia, Harvard Medical School; Anesthetist-in-Chief, Massachusetts General Hospital.* (3, 1940)

Behre, Jeanette Allen, Ph.D. Department of Biochemistry, College of Physicians and Surgeons, 630 W. 168th St., New York City. *Associate.* (2, 1925)

Belding, David L., M.D. Boston University School of Medicine, Boston, Mass. *Professor of Bacteriology and Experimental Pathology.* (4, 1927)

Bell, E. T., M.D. 110 Anatomy Bldg., University of Minnesota, Minneapolis. *Professor of Pathology.* (4, 1931)

Benedict, Francis Gano, Ph.D., Sc.D., M.D. Machiasport, Me. *Former Director of the Nutrition Laboratory of the Carnegie Institution of Washington; Member of the National Academy of Sciences.* (1, 1904; 2, 1906)

Bennett, A. Lawrence, Ph.D., M.D. College of Medicine, University of Nebraska, Omaha. *Professor of Physiology and Pharmacology.* (1, 1941)

Bennett, Granville A., M.D. Tulane University of Louisiana School of Medicine, 1430 Tulane Ave., New Orleans. *Professor of Pathology and Bacteriology.* (4, 1931)

Bennett, Mary Adelia, M.A., Ph.D. Lankenau Hospital Research Institute, Philadelphia, Pa. *Research Biochemist.* (2, 1941)

Benson, Clara C., Ph.D. 157 Bloor St., W., Toronto, Canada. *Professor of Food Chemistry, University of Toronto.* (2, 1906)

Berg, Benjamin N., M.D. 630 W. 168th St., New York City. *Associate in Pathology, Columbia University, College of Physicians and Surgeons.* (4, 1928)

Berg, Clarence P., M.A., Ph.D. Chemistry Department, State University of Iowa, Iowa City. *Associate Professor of Biochemistry.* (2, 1933; 5, 1936)

Berg, William N., Ph.D. 225 W. 106th St., New York City. *Biochemist.* (2, 1906)

Bergeim, Olaf, M.S., Ph.D. 1853 W. Polk St., Chicago, Ill. *Associate Professor of Physiological Chemistry, University of Illinois College of Medicine.* (1, 1916; 2, 1914)

Bergmann, Max, Ph.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member.* (2, 1934)

Bergmann, Werner, Ph.D. Sterling Chemistry Building, Yale University, New Haven, Conn. *Assistant Professor.* (2, 1934)

Berkson, Joseph, M.A., M.D., D.Sc. Mayo Clinic, Rochester, Minn. *Associate Professor, Biometry and Medical Statistics, Mayo Foundation, University of Minnesota.* (1, 1933)

Bernheim, Frederick, Ph.D. Box 3109, Duke Medical School, Durham, N. C. *Associate Professor of Physiology and Pharmacology.* (2, 1933; 3, 1935)

Bernthal, Theodore G., M.S., M.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Associate Professor of Physiology.* (1, 1932)

Berry, George Packer, M.D. University of Rochester, Rochester, N. Y. *Assistant Dean; Professor of Bacteriology; Associate Professor of Medicine.* (4, 1938; 6, 1934)

Bessey, Otto A., Ph.D. Public Health Research Institute of the City of New York, Inc., Park Laby., foot of E. 15th St. *Chief, Division of Nutrition and Physiology.* (2, 1938; 5, 1943)

Best, Charles Herbert, M.A., M.D., D.Sc. (London), D.Sc. (Chicago), F.R.S. University of Toronto, Toronto, Ont., Canada. *Director, Banting and Best Department of Medical Research and Department of Physiology.* (1, 1923; 2, 1923)

Bethell, Frank H., M.D. 409 Lenawee Drive, Ann Arbor, Mich. *Assistant Professor of Internal Medicine and Assistant Director of the Thomas Henry Simpson Memorial Institute.* (4, 1936)

Bethke, Roland M., M.S., Ph.D. Ohio Agricultural Experiment Station, Wooster. *In Charge of Nutritional Investigations.* (2, 1928; 5, 1933)

Beutner, R., M.D., Ph.D. 235 N. 15th St., Philadelphia, Pa. *Professor and Head of Department of Pharmacology, Hahnemann Medical College.* (1, 1924; 3, 1924)

Beyer, Karl H., Jr., Ph.M., Ph.D. Medical Research Division, Sharp & Dohme, Inc., Glenolden, Pa. (1, 1942)

Bieter, Raymond N., M.D., Ph.D. University of Minnesota, Minneapolis. *Professor of Pharmacology.* (3, 1930)

Bills, Charles E., M.A., Ph.D. Mead Johnson & Co., Evansville, Ind. *Director of Research.* (2, 1928; 5, 1935)

Bing, Franklin C., Ph.D. 1135 Fullerton Ave., Chicago, Ill. *Director, American Institute of Baking; Assistant Professor of Physiology, Northwestern University Medical School.* (2, 1931; 5, 1934)

Bing, Richard J., M.D. The Johns Hopkins Hospital, Dept. of Medicine, Baltimore, Md. *Instructor in Medicine, Associate Physician to the Johns Hopkins Hospital.* (1, 1942)

Binger, Carl A., M.D. 125 E. 73rd St., New York City. *Assistant Professor of Clinical Medicine (Psychiatry), Cornell University Medical College.* (1, 1927)

Binkley, Stephen Bennett, M.S., Ph.D. Research Department, Parke, Davis & Co., Detroit, Mich. (2, 1941)

Bisbey, Bertha, A.M., Ph.D. Gwynn Hall, University of Missouri, Columbia. *Professor of Home Economics.* (5, 1933)

Bischoff, Fritz E., M.S., Ph.D. Cottage Hospital, Santa Barbara, Calif. *Director of Research.* (2, 1928; 5, 1933)

p, George H., Ph.D. Washington Univer- Medical School, Euclid and Kingshighway, . Louis, Mo. *Professor of Bio-Physics.* (1, 1923)

Black, Edgar C., Ph.D.* Banting Institute, University of Toronto, Toronto, Ontario, Canada. (1, 1943)

Blair, Edgar A., M.S., Ph.D. U. S. Army, 936 A.B.S. Bn., Camp Rucker, Ala. *Lt. Col.* (1, 1936)

Blair, Henry. A., M.Sc., Ph.D. University of Rochester School of Medicine and Dentistry, Rochester, N. Y. *Associate Professor of Physiology.* (1, 1934)

Blake, Francis G., M.D., M.A. (hon.), Sc.D. Yale University School of Medicine, New Haven, Conn. *Dean and Sterling Professor of Medicine.* (4, prior to 1920; 6, 1921)

Blankenhorn, M. A., M.D. University of Cincinnati, Cincinnati, O. *Professor of Medicine.* (4, 1932)

Blatherwick, Norman R., M.S., Ph.D., Sc.D. Metropolitan Life Ins. Co., 1 Madison Ave., New York City. *Director of Biochemical Laboratory.* (1, 1915; 2, 1915; 5, 1934)

Blau, Nathan F., Ph.D. 1300 York Ave., New York City. (2, 1928)

Bliss, Eleanor A., Sc.D. Department of Preventive Medicine, Johns Hopkins Hospital, 615 N. Wolfe St., Baltimore, Md. *Associate in Preventive Medicine, Johns Hopkins University, School of Medicine.* (6, 1931)

Bliss, Sidney, Ph.D. Tulane University, New Orleans, La. *Professor of Biochemistry, School of Medicine.* (2, 1928)

Block, Richard J., Ph.D. 15 Cooper Rd., Scarsdale, N. Y. *Director of Research, C. M. Armstrong Co.; Associate, Department of Physiology and Biochemistry, New York Medical College, Flower and Fifth Avenue Hospital.* (2, 1934; 5, 1933)

Block, Walter D., M.S., Ph.D. University Hospital, Ann Arbor, Mich. *Instructor in Biological Chemistry, Rackham Arthritis Research Unit.* (2, 1942)

Bloom, William, M.D. 1419 E. 56th St., Chicago, Ill. *Professor of Anatomy, University of Chicago.* (4, 1930)

Bloomfield, A. L., M.D. Stanford University Hospital, San Francisco, Calif. *Professor of Medicine.* (3, 1927; 4, 1927)

Bloor, W. R., A.M., Ph.D. School of Medicine and Dentistry, University of Rochester, Rochester, N. Y. *Professor of Biochemistry.* (1, 1915; 2, 1910)

Blum, Harold F., Ph.D. Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md. *Principal Biologist (Biophysics).* (1, 1928)

Blumberg, Harold, D.Sc. The Johns Hopkins University, Baltimore, Md. *Research Biochemist.* (5, 1942)

Blumenstock, Julius, M.D. Station Hospital, Fort Baker, Calif. *Captain, Medical Corps.* (1, 1925)

Blumgart, Herrmann L., M.D. Beth Israel Hospital, 330 Brookline Ave., Boston, Mass. *Associate Professor of Medicine, Harvard Medical School; Lt. Col., M.C., Hdqtrs., 2nd Service Command, Governor's Island, N. Y.* (1, 1927)

Blunt, Katharine, Ph.D., LL.D. 38 Glenwood Ave., New London, Conn. *President, Retired, Connecticut College for Women.* (2, 1921)

Bock, Joseph C., Ch.E., Ph.D. 561 N. 15th St., Milwaukee, Wis. *Professor of Biochemistry, Marquette University Medical School.* (2, 1916)

Bodansky, Aaron, Ph.D. Hospital for Joint Diseases, 1919 Madison Ave., New York City. *Biological Chemist.* (2, 1926)

Bodansky, Oscar, M.D., Ph.D. Medical Research Laboratory, Edgewood Arsenal, Md. *Captain,*

Medical Corps; Chief, Biochemistry Section, Medical Research Laboratory, Chemical Warfare Service. (2, 1937; 3, 1942)

Bodine, Joseph Hall, Ph.D. State University of Iowa, Iowa City. *Professor and Head of Department of Zoology.* (1, 1925)

De Bodo, Richard C., M.D. 477 First Ave., New York City. *Associate Professor of Pharmacology, New York University College of Medicine.* (1, 1932; 3, 1931)

Boell, Edgar J., Ph.D. Osborn Zoological Laboratory, Yale University, New Haven, Conn. *Associate Professor of Biology.* (1, 1942)

Bogert, L. Jean, Ph.D. Hotel Claremont, Berkeley, Calif. (2, 1917)

Bogert, Marston Taylor, Sc.D., LL.D., R.N.D. Columbia University, New York 27, N. Y. *Professor Emeritus of Organic Chemistry; Member, National Academy of Sciences.* (2, 1925)

Bolliger, Adolph, Ph.D. Gordon Craig Research Laboratories, University of Sydney, Sydney, Australia. *Director of Research.* (2, 1928)

Bollman, J. L., M.D. Mayo Clinic, Rochester, Minn. *Associate in Division of Experimental Surgery and Pathology, Mayo Clinic; Professor of Physiology, Mayo Foundation, University of Minnesota.* (4, 1927)

Bond, Glenn C., Ph.D., M.D. The Upjohn Co., Research Laboratories, Kalamazoo, Mich. (6, 1939)

Booher, Lela E., Ph.D. General Mills, Inc., Minneapolis, Minn. *Chief Nutritionist.* (2, 1933; 5, 1933)

Bookman, Samuel, M.A., Ph.D. 624 Madison Ave., New York City. *Consulting Chemist, Mt. Sinai Hospital.* (2, 1912)

Boor, Alden K., M.S., Ph.D. Department of Medicine, University of Chicago, Chicago, Ill. *Assistant Professor of Biochemistry.* (2, 1931)

Boothby, W. M., M.D., M.A., F.A.C.S. Metabolism Laboratory, The Mayo Clinic, Rochester, Minn. *Chief of Section of Clinical Metabolism in Division of Medicine, Mayo Clinic; Professor of Experimental Metabolism, Mayo Foundation, University of Minnesota; Chairman, Mayo Aero-Medical Unit.* (1, 1915; 2, 1920; 3, 1923; 4, 1924)

Bordley, James, III, M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Medicine, Johns Hopkins University.* (1, 1938)

Borsook, Henry, M.D., Ph.D. California Institute of Technology, Pasadena 4. *Professor of Biochemistry.* (2, 1931)

Bosworth, Alfred Willson, A.M., M.D. R. D. 4, Circleville, O. *Consulting Chemist.* (2, 1936; 5, 1935)

Bott, Phyllis A., M.S., Ph.D. Woman's Medical College of Pennsylvania, East Falls, Philadelphia. *Associate Professor of Physiological Chemistry.* (2, 1938)

Bouman, H. D., M.D.* University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. *Assistant Professor of Psychology; Research Fellow in Orthopedic Surgery.* (1, 1943)

Bourne, Wesley, M.D., C.M., M.Sc., F.R.C.P., D.A. (R.C.P. & S., Eng.). McGill University, Montreal, Canada. *Lecturer in Anesthetics, Dept. of Pharmacology and Therapeutics.* (3, 1936)

Bourquin, Helen, M.S., Ph.D. 923 N. Nevada Ave., Colorado Springs, Colo. (1, 1925)

Boyd, Eldon M., M.A., M.D., C.M. Queen's University, Kingston, Ontario, Canada. *Professor and Head of the Department of Pharmacology.* (3, 1941)

Boyd, T. E., Ph.D. 706 S. Lincoln St., Chicago, Ill. *Professor of Physiology, Loyola University, School of Medicine.* (1, 1924)

Boyd, William C., A.M., Ph.D. Boston University School of Medicine, 80 E. Concord St., Boston, Mass. *Associate Professor of Biochemistry.* (2, 1940; 6, 1933)

Boyden, Edward A., A.M., Ph.D. University of Minnesota, Minneapolis. *Professor of Anatomy.* (1, 1929)

Boyle, Paul E., D.M.D. 25 Shattuck St., Boston, Mass. *Assistant Professor of Oral Pathology and Clinical Dentistry, Harvard School of Dental Medicine.* (4, 1939)

Bozler, Emil, Ph.D. Ohio State University, Columbus. *Assistant Professor of Physiology.* (1, 1932)

Bradbury, James T., M.S., Sc.D. Bureau of Dairy Industry, U. S. Department of Agriculture, Beltsville, Md. *Endocrinologist.* (1, 1941)

Bradley, Harold C., Ph.D. Memorial Institute Bldg., Madison, Wis. *Professor of Physiological Chemistry, University of Wisconsin.* (1, 1911; 2, 1908)

Bradley, William B., Ph.D. 3646 Lafayette Ave., Omaha, Neb. (1, 1939)

Branch, Charles F., M.D. Boston University School of Medicine, 80 E. Concord St., Boston, Mass. *Professor of Pathology.* (4, 1940)

Branch, E. Arnold G., M.D. Bureau of Laboratories, General Hospital, St. John, N. B. *Director; Acting Director, Bureau of Laboratories, New Brunswick Department of Health.* (4, 1929)

Brand, Erwin, Ph.D. 630 W. 168th St., New York City. *Associate Professor of Biological Chemistry, Columbia University.* (2, 1929)

Brandes, W. W., M.D. Roosevelt Hospital, W. 59th St., New York City. (4, 1931)

Branham, Sara E., Ph.D., M.D., Sc.D. National Institute of Health, 25th and E Sts., N.W.,

Washington, D. C. *Senior Bacteriologist.* (6, 1926)

Branion, Hugh Douglas, M.A., Ph.D. 50 James St., Guelph, Canada. (5, 1933)

Brassfield, Charles R., Ph.D. University of Michigan, Ann Arbor. *Assistant Professor of Physiology.* (1, 1937)

Bratton, Andrew Calvin, Jr., M.A., Ph.D. Johns Hopkins School of Medicine, Baltimore, Md. *Associate in Pharmacology.* (3, 1941)

Braun, Herbert A., Ph.D. Food & Drug Administration, Federal Security Agency, Washington, D. C. *Associate Pharmacologist.* (3, 1941)

Brewer, George, M.D. University of Pennsylvania, School of Medicine, Philadelphia. *Assistant Professor of Physiology.* (1, 1937)

Bridge, Edward M., M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate in Pediatrics, Johns Hopkins University.* (2, 1940)

Briggs, A. P., M.D. University of Georgia, Augusta. *Associate Professor in Biochemistry and Medicine.* (2, 1923)

Brink, Frank, Jr., Ph.D. Johnson Research Foundation, University of Pennsylvania, Philadelphia. *Fellow in Medical Physics, Johnson Research Foundation; Lecturer in Biophysics, Graduate School, University of Pennsylvania.* (1, 1942)

Brinkhous, K. M., M.D. State University of Iowa, Department of Pathology, Medical Laboratories Building, Iowa City. *Assistant Professor of Pathology.* (4, 1939)

Britton, Sydney W., M.D. University of Virginia School of Medicine, University. *Professor of Physiology.* (1, 1925)

Brobeck, John R., M.D., Ph.D.* Yale University School of Medicine, New Haven, Conn. *Instructor, Laboratory of Physiology.* (1, 1943)

Brodie, Bernard B., Ph.D. New York University Research Service, Welfare Hospital, Welfare Island, New York City. *Research Assistant in Biochemistry and Instructor in Medicine.* (2, 1940)

Brody, Samuel, M.A., Ph.D. Dairy Building, University of Missouri, Columbia. *Associate Professor, College of Agriculture and Agricultural Experiment Station.* (2, 1929; 5, 1933)

Bronfenbrenner, J. J., Ph.D., D.P.H. Washington University School of Medicine, St. Louis, Mo. *Professor of Bacteriology and Immunology.* (4, 1940; 6, 1918)

Bronk, Detlev W., M.S., Ph.D., Sc.D. The Eldridge Reeves Johnson Foundation for Medical Physics, University of Pennsylvania, Philadelphia. *Johnson Professor of Biophysics and Director, Johnson Foundation; Member National Academy of Sciences.* (1, 1927)

Brookes, Margaret C. Hessler, A.M., Ph.D. University of Chicago, Chicago, Ill. *Assistant Professor, Department of Home Economics.* (5, 1935)

Brooks, Chandler McCuskey, M.A., Ph.D. Johns Hopkins University School of Medicine, Baltimore, Md. *Associate Professor of Physiology.* (1, 1934)

Brooks, Clyde, Ph.D., M.D., LL.D. Louisiana State Univ. Medical Center, New Orleans. *Professor of Physiology and Pharmacology.* (1, 1910; 3, 1912)

Brooks, Matilda Moldenhauer, M.S., Ph.D. Department of Zoology, University of California, Berkeley. *Research Associate in Biology.* (1, 1923)

Brooks, Sumner Cushing, Ph.D. University of California, Berkeley. *Professor of Zoology.* (1, 1923)

Broun, Goronwy Owen, M.D. 1325 S. Grand Blvd., St. Louis, Mo. *Professor of Internal Medicine, St. Louis University.* (4, 1927)

Brown, Aaron, M.D. 39 West 55th St., New York City. *Assistant Clinical Professor of Medicine, New York University College of Medicine.* (6, 1923)

Brown, Claude P., M.D. 1930 Chestnut St., Philadelphia, Pa. *Assistant Director, Pennsylvania State Board of Health Laboratories.* (6, 1913)

Brown, Dugald E. S., M.A., Ph.D. New York University College of Dentistry, 209 E. 23rd St., New York City. *Professor of Physiology.* (1, 1932)

Brown, Edgar D., Pharm.D., M.D. Paynesville, Minn. *Associate Professor of Pharmacology Emeritus.* (1, 1907; 3, 1909)

Brown, Frank A., Jr., M.A., Ph.D. Zoological Laboratories, Northwestern University, Evanston, Ill. *Associate Professor of Zoology.* (1, 1940)

Brown, John B., M.S., Ph.D. Ohio State University, Columbus. *Professor of Physiological Chemistry.* (2, 1927; 5, 1934)

Brown, Rachel, M.S., Ph.D. 26 Buckingham Drive, Albany, N. Y. *Senior Biochemist, Division of Laboratories and Research, New York State Department of Health.* (6, 1933)

Browne, J. S. L., M.D., Ph.D., F.R.S.C. University Clinic, Royal Victoria Hospital, Montreal, Canada. *Assistant Professor of Medicine, McGill University.* (1, 1934)

Brownell, Katharine A., M.A., Ph.D.* Department of Physiology, Ohio State University, Columbus. *Research Associate.* (1, 1943)

Brues, Austin M., M.D. 695 Huntington Ave., Boston, Mass. *Assistant Professor of Medicine, Harvard Medical School; Assistant Physician, Mass. General Hospital.* (1, 1940)

Bruger, Maurice, M.D., C.M., M.Sc. 301 E. 20th St., New York 3, N. Y. *Associate Clinical*

Professor of Medicine, New York Post-Graduate Medical School of Columbia University; Chief, Division of Pathological Chemistry, New York Post-Graduate Hospital. (2, 1935; 5, 1935)

Bruhn, John M., Ph.D. University of Alabama School of Medicine, University. *Associate Professor of Physiology and Pharmacology.* (1, 1939)

Brunschwig, Alexander, M.D. University of Chicago, Chicago, Ill. *Professor of Surgery.* (4, 1937)

Bryan, W. Ray, Ph.D. 5516 Johnson Ave., Bethesda, Md. *Biologist, National Cancer Institute.* (1, 1934; 4, 1940)

Buchanan, J. William, Ph.D. Northwestern University, Evanston, Ill. *Professor of Zoology.* (1, 1927)

Buchbinder, Leon, Ph.D. Department of Health, 125 Worth St., New York City. (6, 1934)

Buchbinder, William C., M.S., M.D. 104 S. Michigan Ave., Chicago, Ill. *Assistant Professor of Medicine, Northwestern University Medical School; Associate in Medicine, Michael Reese Hospital.* (1, 1940)

Buckner, G. Davis, Ph.D. Kentucky Agricultural Experiment Station, Lexington. *In Charge of Animal Nutrition.* (2, 1920)

Bucy, Paul C., M.S., M.D. 25 E. Washington St., Chicago, Ill. *Associate Professor of Neurology and Neurological Surgery, University of Illinois.* (1, 1933)

Buddingh, G. John, M.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Associate Professor of Bacteriology.* (4, 1940)

Buell, Mary Van Rensselaer, Ph.D. Johns Hopkins Hospital, Baltimore, Md. *Associate in Medicine.* (2, 1921)

Bugbee, Edwin P., M.D. Lankenau Hospital, Philadelphia, Pa. *Assistant Roentgenologist.* (1, 1928)

Bugher, John C., M.D. Apartado 2508, Bogota, Columbia, South America. (4, 1935)

Bulatao, Emilio, M.D. University of the Philippines, Manila, P.I. *Professor of Physiology.* (1, 1924)

Bulger, Harold A., Ph.D., M.D. Barnes Hospital, 600 S. Kingshighway, St. Louis, Mo. *Assistant Professor of Medicine, Washington University.* (5, 1933)

Bull, Henry B., Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Associate Professor, Department of Chemistry.* (2, 1937)

Bunde, Carl A., M.A., Ph.D.* Southwestern Medical Foundation, Dallas, Texas. *Associate Professor of Physiology and Pharmacology.* (1, 1943)

Bunney, William E., Ph.D. E. R. Squibb & Sons, New Brunswick, N. J. *Director of Biologic Products Production.* (6, 1931)

Bunting, Charles H., M.D. Service Memorial Institute, Madison, Wis. *Professor of Pathology, University of Wisconsin.* (4, prior to 1920)

Bunzell, H. H., Ph.D. Box 44, General Post Office, New York 1, N. Y. *Director, Bunzell Laboratories.* (2, 1908)

Burchell, Howard B., M.D., Ph.D. Mayo Clinic, Rochester, Minn. *Instructor in Medicine, Mayo Foundation, Graduate School, University of Minnesota; Consultant in Medicine, Mayo Clinic, Rochester, Minn.* (1, 1942)

Burdick, H. O., M.A., Sc.D. (hon.). Alfred University, Alfred, N. Y. *Professor of Biology.* (1, 1940)

Burdon, Kenneth L., Sc.M., Ph.D. Louisiana State University Medical Center, New Orleans. *Assistant Professor of Immunology and Bacteriology; Consultant, United States Public Health Service.* (6, 1936)

Burge, W. E., A.M., Ph.D. University of Illinois, Urbana. *Associate Professor of Physiology.* (1, 1911)

Burk, Dean, Ph.D. National Cancer Institute, U. S. Public Health Service, Bethesda, Md. *Senior Chemist.* (2, 1939)

Burky, Earl L., M.S., M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Ophthalmology, Wilmer Institute of Ophthalmology, Johns Hopkins University.* (6, 1931)

Burnett, Theo. C., M.D. Box 216, Carmel, Calif. *Associate Professor of Physiology Emeritus, University of California.* (1, 1911)

Burns, Edward L., M.D. Louisiana State University, School of Medicine, New Orleans. *Associate Professor of Pathology and Bacteriology.* (4, 1939)

Burr, George O., M.A., Ph.D., LL.D. University of Minnesota, Minneapolis. *Director Division of Physiological Chemistry.* (2, 1928; 5, 1933)

Burrows, Montrose T., M.D. 201 N. El Molino Ave., Pasadena, Calif. (4, prior to 1920)

Burton, Alan C., Ph.D. Banting Institute, Toronto, Canada. (1, 1937)

Burton-Opitz, Russell, M.S., M.D., Ph.D. 218 Bridle Way, Palisade, N. J. *Attending Cardiologist, Lenox Hill Hospital; Attending Physician, Cumberland Hospital; Consulting Cardiologist, Engelwood, North Hudson, Holy Name and Hackensack Hospitals.* (1, 1902; 2, 1906; 3, 1919)

Bush, Milton T., Ph.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Research Associate in Pharmacology.* (3, 1938)

Butler, Thomas C., M.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Assistant Professor of Pharmacology.* (3, 1938)

Butt, Hugh R., M.D. U. S. Naval Hospital, Corona, Calif. (5, 1942)

Butts, Joseph S., M.S., Ph.D. A.P.O. 633, % Postmaster New York City. *Major, 8th Air Force Hq., Medical.* (2, 1936; 5, 1936)

Butz, Eleanore W. J., Ph.D. Beltsville, Md. *Collaborator, Div. Animal Husbandry, U. S. D. A., Beltsville Research Center.* (6, 1935)

Cahill, William M., Ph.D. Wayne University College of Medicine, Detroit, Mich. *Assistant Professor of Physiological Chemistry.* (2, 1940)

Cajori, Florian A. Ph.D. 407 N. Wayne Ave., Wayne, Pa. *Major, Sanitary Corps, U. S. Army; Assistant Professor of Physiological Chemistry, University of Pennsylvania Medical School.* (2, 1922; 5, 1933)

Caldwell, Mary L., A.M., Ph.D. Department of Chemistry, Columbia University, New York City. *Associate Professor of Chemistry.* (2, 1924; 5, 1933)

Calvery, Herbert O., M.S., Ph.D. Food and Drug Administration, Federal Security Agency, Washington 25, D. C. *Chief, Division of Pharmacology.* (2, 1928; 3, 1939)

Calvin, D. Bailey, M.A., Ph.D. School of Medicine, University of Texas, Galveston. *Associate Professor of Biological Chemistry.* (1, 1934; 2, 1939)

Cameron, A. T., M.A., D.Sc., F.I.C., F.R.S.C. Medical College, Winnipeg, Manitoba, Canada. *Professor of Biochemistry, Faculty of Medicine, University of Manitoba; Biochemist, Winnipeg General Hospital.* (1, 1914; 2, 1914)

Camp, Walter J. R., M.D., Ph.D. 1853 Polk St., Chicago, Ill. *Professor of Pharmacology and Therapeutics, University of Illinois.* (3, 1926)

Campbell, Dan H., M.S., Ph.D. Department of Chemistry, California Institute of Technology, Pasadena, Calif. *Assistant Professor of Immunochemistry.* (6, 1938)

Campbell, H. Louise, Ph.D. 435 W. 119th St., Apt. 9-F, New York City. *Research Assistant in Food Chemistry, Columbia University.* (5, 1933)

Campbell, James, M.A., Ph.D.* University of Toronto, Toronto, Ontario, Canada. *Assistant Professor of Physiology. Lieutenant Commander, (S.B.) R.C.N.V.R.* (1, 1943)

Campbell, Walter Ruggles, M.A., M.D., F.R.C.P. (C), F.R.S.C. 69 Madison Ave., Toronto, Canada. *Assistant Professor of Medicine and Clinical Medicine, University of Toronto; Assistant Physician, Toronto General Hospital.* (2, 1922)

Cannan, R. Keith, D.Sc. 477 First Ave., New York City. *Professor of Chemistry, New York University College of Medicine.* (2, 1931)

Cannon, Paul R., M.D., Ph.D. University of Chicago, Chicago, Ill. *Professor of Pathology.* (4, 1930; 6, 1929)

Cannon, Walter B., A.M., M.D., Sc.D., LL.D. Harvard Medical School, Boston, Mass. *George Higginson Professor of Physiology, Harvard University; Member of the National Academy of Sciences.* (1, 1900)

Cantarow, Abraham, M.D. Jefferson Medical College, Philadelphia, Pa. *Associate Professor of Medicine; Biochemist to the Jefferson Hospital.* (1, 1932; 3, 1935)

Canzanelli, Attilio, M.D. Tufts College Medical School, 416 Huntington Ave., Boston, Mass. *Associate Professor in the Department of Physiology.* (1, 1934)

Carlson, A. J., A.M., Ph.D., M.D., LL.D. Hull Physiological Laboratory, University of Chicago, Chicago, Ill. *Professor of Physiology Emeritus; Member of the National Academy of Sciences.* (1, 1904; 5, 1933)

Carmichael, Emmett B., Ph.D. School of Medicine, University of Alabama, University. *Professor of Physiological Chemistry.* (1, 1931)

Carmichael, Leonard, Ph.D., Sc.D., Litt.D., LL.D. Tufts College, Medford, Mass. *Director, the Tufts College Research Laboratory of Sensory Psychology and Physiology and President of the College.* (1, 1937)

Carpenter, Thorne M., Ph.D. 29 Blackfon St., Boston, 15, Mass. *Director, Nutrition Laboratory of the Carnegie Institution of Washington.* (1, 1915; 2, 1909; 5, 1935)

Carr, C. Jelleff, Ph.D. School of Medicine, University of Maryland, Baltimore. *Associate Professor of Pharmacology.* (3, 1940)

Carr, Jesse L., M.D. University of California Medical School, Third and Parnassus Aves., San Francisco. *Assistant Professor of Pathology.* (4, 1940)

Carrel, Alexis, M.D., Sc.D., LL.D. The Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member Emeritus.* (1, 1906; 4, 1924)

Carter, Herbert E., M.A., Ph.D. 452 Noyes Laboratory, Urbana, Ill. *Associate Professor of Biochemistry, University of Illinois.* (2, 1937; 5, 1941)

Cartland, George F., M.S., Ph.D. The Upjohn Co., Research Department, Kalamazoo, Mich. *Biochemist and Pharmacologist.* (2, 1936)

Cary, Charles A., S.B. Dairy Research Laboratory, Beltsville, Md. *Chief, Division of Nutrition and Physiology, Bureau of Dairy Industry, U. S. Department of Agriculture.* (2, 1920)

Casey, Albert Eugene, M.D. Jefferson and Baptist Hospitals, Birmingham, Ala. *Pathologist.* (4, 1933)

Cash, James Robert, M.D. University Hospital, Charlottesville, Va. *Professor of Pathology, University of Virginia.* (4, 1924)

Castle, Edward S., M.A., Ph.D. Biological Laboratories, Harvard University, Divinity Ave.,

Cambridge, Mass. *Assistant Professor of General Physiology.* (1, 1934)

Castle, William B., M.D., S.M. (Hon. Yale), M.D. (Hon. Utrecht). Boston City Hospital, Boston, Mass. *Professor of Medicine, Harvard Medical School; Associate Director, Thorndike Memorial Laboratory and Director, II and IV Medical Services (Harvard), Boston City Hospital.* (4, 1942)

Catchpole, Hubert Ralph, Ph.D. 333 Cedar St., New Haven, Conn. *Research Assistant in Physiology (Assistant Professor), Yale University.* (1, 1941)

Cathcart, E. P., M.D., D.Sc., LL.D. University of Glasgow, Glasgow, Scotland. *Dean of University.* (5, 1935)

Catron, Lloyd, M.D. The City Hospital, Akron, O. *Pathologist.* (4, 1939)

Cattell, J. McKeen, Ph.D., D.Sc., LL.D. Garrison-on-Hudson, N. Y. *Editor of Science, The Scientific Monthly, The American Naturalist, and School and Society; Member of the National Academy of Sciences.* (1, 1895)

Cattell, McKeen, A.M., Ph.D., M.D. Cornell University Medical College, 1300 York Ave., New York City. *Professor of Pharmacology.* 1, 1923; 3, 1924)

Cerecedo, Leopold R., Ph.D. Fordham University, New York City. *Professor of Biochemistry.* (2, 1931)

Chaikoff, I. L., A.M., Ph.D., M.D. University of California, Berkeley. *Assistant Professor of Physiology.* (1, 1932)

Chalkley, Harold W., A.M., Ph.D. U. S. Public Health Service, National Institute of Health, Bethesda, Md. *Senior Physiologist.* (1, 1932)

Chambers, Leslie Addison, M.S., Ph.D. Johnson Foundation for Medical Physics, University of Pennsylvania, Philadelphia. *Lecturer in Biophysics; Associate in Medical Physics; Associate in Pediatrics.* (1, 1940)

Chambers, Robert, A.M., Ph.D. New York University, Washington Square East, New York City. *Research Professor of Biology.* (1, 1932)

Chambers, William H., M.S., Ph.D. Cornell University Medical College, 1300 York Ave., New York City. *Associate Professor of Physiology.* (1, 1924; 5, 1933)

Chandler, Caroline A., M.D. Children's Bureau, U. S. Department of Labor, Washington, D. C. (6, 1938)

Chanutin, Alfred, Ph.D. Box 1038 (University Station), Charlottesville, Va. *Professor of Biochemistry, University of Virginia.* (2, 1925)

Chapman, C. W., M.Sc., Ph.D. University of Maryland, Baltimore. *Professor of Pharmacology.* (3, 1932)

Chargaff, Erwin, Ph.D. Columbia University, College of Physicians and Surgeons, 630 W. 168th St., New York City. *Assistant Professor of Biological Chemistry.* (2, 1935)

Charipper, Harry Adolph, M.S., Ph.D. Washington Square College of Arts and Sciences, 100 Washington Square East, New York City. *Professor of Biology and Chairman of the Department.* (1, 1941)

Chase, Aurin M., A.M., Ph.D. Department of Biology, Princeton University, Princeton, N. J. *Research Associate.* (1, 1939)

Chase, Merrill W., M.S., Ph.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Member of Staff.* (6, 1938)

Chasis, Herbert, M.D., Med. Sc.D. 44 E. 67th St., New York City. *Assistant Professor of Medicine, New York University, College of Medicine.* (1, 1941)

Chatfield, Charlotte, B.S. U. S. Dept. of Agriculture, Washington, D. C. *In Charge, Food Composition Section, Bureau of Home Economics.* (5, 1941)

Chen, K. K., Ph.D., M.D. Eli Lilly and Co., Indianapolis, Ind. *Director of Pharmacological Research, Lilly Research Laboratories; Professor of Pharmacology, Indiana University School of Medicine, Indianapolis.* (1, 1929; 3, 1942)

Cheney, Ralph H., A.M., M.S., Sc.D. Long Island University, 300 Pearl St., Brooklyn, N. Y. *Chairman, Biology Department.* (3, 1934)

Chesney, Alan M., M.D. The Johns Hopkins Hospital, Baltimore, Md. *Dean, Johns Hopkins Medical School; Associate Professor of Medicine.* (4, 1925)

Child, Charles Manning, Ph.D., D.Sc. (hon.). Jordon Hall, Stanford University, Calif. *Member, National Academy of Sciences; Professor Emeritus, University of Chicago.* (1, 1923)

Chittenden, Russell H., Ph.D., LL.D., Sc.D., M.D. 83 Trumbull St., New Haven, Conn. *Professor Emeritus, Physiological Chemistry, Yale University; Member, National Academy of Sciences.* (1, 1887; 2, 1906; 5, 1933)

Chow, Bacon, Ph.D. Squibb Institute for Medical Research, New Brunswick, N. J. *Associate in the Division of Pharmacology.* (2, 1940)

Christensen, L. Royal, Ph.D. New York University College of Medicine, 477 First Ave., New York City. *Medical Fellow, National Research Council.* (6, 1942)

Christian, Henry A., M.D. 1731 Beacon St., Brookline, Mass. *Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University; Physician-in-Chief, Emeritus, Peter Bent Brigham Hospital, Boston; Visiting Physician, Beth Israel Hospital, Boston.* (4, 1924)

Christman, Adam A., Ph.D. University of Michigan Medical School, Ann Arbor. *Associate Professor of Physiological Chemistry.* (2, 1929)

Clark, Ada R., M.A., Ph.D. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Instructor in Bacteriology.* (6, 1936)

Clark, Byron B., M.S., Ph.D. Albany Medical College, Albany, N. Y. *Associate Professor of Physiology and Pharmacology.* (3, 1940)

Clark, Earl P., M.S., Ph.D. Bureau of Entomology and Plant Quarantine, U. S. Dept. of Agriculture, Washington 25, D. C. *Senior Chemist.* (2, 1924)

Clark, Eliot R., M.D. University of Pennsylvania, Philadelphia. *Professor and Head of Department of Anatomy.* (1, 1919)

Clark, Ernest D., A.M., Ph.D. 826 Skinner Bldg., Seattle 1, Wash. *Director of the Laboratories, Northwest Branch, National Canners' Association; Manager, Association Pacific Fisheries.* (2, 1912)

Clark, George, Ph.D.* Yerkes Laboratory of Primate Biology, Orange Park, Fla. *Research Associate.* (1, 1943)

Clark, Guy W., A.M., Ph.D. c/o Lederle Laboratories, Inc., Pearl River, N. Y. *Technical Director.* (2, 1922)

Clark, Janet Howell, A.M., Ph.D. Anderson Hall, University of Rochester, Rochester, N. Y. *Dean of the College for Women and Professor in the Division of Biological Sciences.* (1, 1922)

Clark, Paul F., Ph.D. University of Wisconsin Medical School, Madison. *Professor of Bacteriology.* (4, 1923; 6, 1928)

Clark, William G., Ph.D. University of Minnesota, Minneapolis. *Assistant Professor of Zoology.* (1, 1942)

Clark, William Mansfield, M.A., Ph.D., D.Sc. Johns Hopkins University, Baltimore, Md. *Professor of Physiological Chemistry; Member National Academy of Sciences.* (2, 1920)

Clarke, Hans Thacher, D.Sc. (London), F.I.C. 630 W. 168th St., New York City. *Professor of Biological Chemistry, Columbia University, College of Physicians and Surgeons.* (2, 1929)

Clarke, Robert W., Ph.D. Yale University School of Medicine, 333 Cedar St., New Haven, Conn. *Instructor in Physiology.* (1, 1936)

Clausen, Samuel Wolcott, M.D. Strong Memorial Hospital, Rochester, N. Y. *Professor of Pediatrics, School of Medicine, University of Rochester.* (2, 1922)

Cleghorn, Robert Allen, M.D., D.Sc. (Aberdeen). Department of Medicine, University of Toronto, Toronto, Ont., Canada. *Junior Demonstrator in Medicine; Junior Assistant Attending Physician, Toronto General Hospital.* (1, 1937)

Climenko, David Robert, M.D., Ph.D. Winthrop Chemical Co., 33 Riverside Ave., Rensselaer, N. Y. *Pharmacologist; Associate in Biochemistry and Instructor in Medicine, Albany Medical College.* (1, 1933)

Clowes, George Henry Alexander, Ph.D., D.Sc. (hon.), LL.D. (hon.). Eli Lilly & Co., Indianapolis, Ind. *Director of Research.* (2, 1914; 6, 1919)

Coca, Arthur F., A.M., M.D. Pearl River, N. Y. *Medical Director, Lederle Laboratories.* (6, 1916)

Code, Charles F., Ph.D., M.D. Mayo Foundation, Rochester, Minn. *Professor of Physiology.* (1, 1939)

Coffey, Julia M., A.B. Division of Laboratories & Research, New York State Department of Health, Albany, N. Y. *Associate Bacteriologist.* (6, 1937)

Coghill, Robert D., M.S., Ph.D. Northern Regional Research Laboratory, U. S. Department of Agriculture, Peoria, Ill. *Chief, Fermentation Division.* (2, 1932)

Cohen, Barnett, M.S., Ph.D. Johns Hopkins University School of Medicine, 710 N. Washington St., Baltimore 5, Md. *Associate Professor of Physiological Chemistry.* (2, 1935)

Cohen, Milton B., M.D. 10616 Euclid Ave., Cleveland, O. *Director, The Asthma, Hay Fever and Allergy Foundation.* (6, 1931)

Cohen, Philip P., Ph.D., M.D. Service Memorial Institute, University of Wisconsin, Madison. *Assistant Professor of Clinical Chemistry.* (2, 1941)

Cohen, Sophia M., B.S. Division of Laboratories and Research, New York State Department of Health, Albany, N. Y. *Assistant Bacteriologist.* (6, 1938)

Cohn, Alfred E., M.D. 300 Central Park W., New York City. *Member, Rockefeller Institute for Medical Research.* (1, 1911; 3, 1913)

Cohn, Edwin J., Ph.D. 183 Brattle St., Cambridge, Mass. *Professor of Biological Chemistry, Harvard University.* (1, 1919; 2, 1919)

Cole, Arthur G., Ph.D. 1853 W. Polk St., Chicago 12, Ill. *Assistant Professor of Physiological Chemistry, University of Illinois College of Medicine.* (2, 1939)

Cole, Harold N., M.D. 1352 Hanna Bldg., Cleveland, O. *Clinical Professor of Dermatology and Syphilology, Western Reserve University.* (3, 1925)

Cole, Kenneth S., Ph.D. 630 W. 168th St., New York City. *Associate Professor of Physiology, College of Physicians and Surgeons, Columbia University.* (1, 1934)

Cole, Rufus, M.D., D.Sc. Mount Kisco, N. Y. *Member Emeritus, Rockefeller Institute for Medical Research.* (4, 1924; 6, 1917)

Cole, Versa V., Ph.D., M.D. Woman's Medical College, Henry Ave., & Abbottsford Rd., Philadelphia, Pa. *Associate Professor of Pharmacology.* (3, 1941)

Collett, Mary Elizabeth, A.M., Ph.D. Mather College, Western Reserve University, Cleveland, O. *Associate Professor of Biology.* (1, 1921)

Collins, Dean A., M.A., Ph.D., M.D. Temple University School of Medicine, Philadelphia, Pa. *Associate Professor of Physiology.* (1, 1938)

Collins, Russell J., A.M., M.D., F.R.C.P. (Can.) M.R.C.P. (Edin.) F.A.C.P. St. John, New Brunswick, Canada. *Medical Superintendent of St. John Tuberculosis Hospital.* (3, 1915)

Collip, J. B., A.M., Ph.D., D.Sc., M.D. McGill University, Montreal, Quebec, Canada. *Professor of Biochemistry and Director of Research Institute of Endocrinology.* (1, 1920; 2, 1920)

Coman, Dale R., M.D. McManes Laboratory of Pathology, University of Pennsylvania School of Medicine, Philadelphia. *Assistant Professor of Pathology.* (4, 1939)

Comroe, Julius H., Jr., M.D. University of Pennsylvania Medical School, Philadelphia. *Assistant Professor of Pharmacology.* (3, 1939)

Conant, James B., Ph.D. 5 University Hall, Cambridge, Mass. *President, Harvard University; Member, National Academy of Sciences.* (2, 1932)

Concepcion, Isabelo, M.D. College of Medicine and Surgery, Manila, P.I. *Professor of Physiology, University of the Philippines.* (1, 1919)

Conklin, Ruth E., M.S., Ph.D. Vassar College. Poughkeepsie, N. Y. *Associate Professor of Physiology.* (1, 1940)

Conn, Jerome W., M.D. University Hospital, Ann Arbor, Mich. *Assistant Professor of Internal Medicine and Research Associate in Nutrition.* (5, 1942)

Cook, Donald Hunter, Ph.D. School of Tropical Medicine of Columbia University, San Juan, Puerto Rico. *Associate Professor of Chemistry.* (2, 1929)

Cooke, Robert A., A.M., Sc.D. (hon.), M.D. 60 E. 58th St., New York City. *Director, Department of Allergy, Roosevelt Hospital.* (6, 1920)

Cooley, Thomas B., M.S., M.D. 7840 Van Dyke Pl., Detroit, Mich. *Chairman of Staff, Children's Hospital of Michigan, Detroit.* (5, 1935)

Coolidge, Thomas B., M.D., Ph.D. Duke Hospital, Durham, N. C. *Assistant Professor of Biochemistry, Duke University Medical School.* (2, 1942)

Coombs, Helen C., A.M., Ph.D. Department of Hygiene, Brooklyn College, Bedford Ave. and Ave. H., Brooklyn, N. Y. *Instructor in Physiology and Nutrition.* (1, 1921; 3, 1939)

Coon, Julius M., Ph.D. University of Chicago, Chicago, Ill. *Instructor in Pharmacology.* (3, 1941)

Coons, Callie Mae, Ph.D. 1200 W. 78th St., Los Angeles, Calif. (5, 1933)

Cope, Otis M., M.D. New York Medical College, Flower and Fifth Avenue Hospitals, No. 1, E. 105th St., New York City. *Professor of Physiology and Biochemistry.* (1, 1929)

Corbin, Kendall B., M.D. University of Tennessee College of Medicine, 875 Monroe, Memphis. *Professor of Anatomy.* (1, 1941)

Corcoran, Arthur Curtis, C.M., M.D. Lilly Laboratory for Clinical Research, Indianapolis City Hospital, Indianapolis, Ind. *Member of Staff.* (1, 1940)

Corey, Edward Lyman, Ph.D. School of Medicine, University of Virginia, University. *Assistant Professor of Physiology.* (1, 1931)

Cori, Carl F., M.D. Washington University School of Medicine, Kingshighway and Euclid Ave., St. Louis, Mo. *Professor of Pharmacology and Biochemistry; Member, National Academy of Sciences.* (2, 1925; 3, 1934)

Cori, Gerty T., M.D. Washington University School of Medicine, St. Louis, Mo. *Research Associate Professor in Pharmacology and Biochemistry.* (2, 1927; 3, 1934)

Corley, Ralph Conner, Ph.D. Department of Chemistry, Purdue University, Lafayette, Ind. *Professor of Biochemistry.* (2, 1927)

Cornwall, Leon, M.D. 55 E. 76th St., New York City. *Attending Neurologist, N. Y. Neurological Institute.* (6, 1920)

Corper, Harry J., M.D., Ph.D. 1295 Clermont St., Denver, Colo. *Director of Research, National Jewish Hospital.* (2, 1912)

Corson, Samuel A., M.S., Ph.D.* The University of Oklahoma, School of Medicine, Oklahoma City. *Assistant Professor of Physiology.* (1, 1943)

Corwin, Warren C., M.D. Captain, M.C. AUS Army Flying School, Greenville, Miss. (4, 1940)

Co Tui, Frank, M.D. New York University College of Medicine, 477 First Ave., New York City. *Associate Professor of Experimental Surgery.* (3, 1931)

Cowgill, George Raymond, Ph.D. 333 Cedar St., New Haven, Conn. *Associate Professor of Physiological Chemistry, Yale University.* (1, 1923; 2, 1922; 5, 1933)

Cox, Gerald J., M.S., Ph.D. 3803 S St., N. W., Washington 7, D. C. *Special Research Assistant, Food and Nutrition Board, National Research Council.* (2, 1930; 5, 1935)

Cox, Warren M., Jr., Ph.D. Mead Johnson & Co., Evansville, Ind. *Research Biochemist.* (2, 1935)

Craig, L. C., M.S., Ph.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Associate in Chemical Pharmacology.* (2, 1938)

Crampton, E. W., Ph.D. Macdonald College, Quebec, Canada. *Associate Professor of Animal Nutrition.* (5, 1940)

Crandall, Lathan A., Jr., M.D., Ph.D. University of Tennessee College of Medicine, Memphis. *Professor of Physiology.* (1, 1930; 5, 1940)

Cretcher, Leonard H., Ph.D. Mellon Institute of Industrial Research, University of Pittsburgh, Pittsburgh, Pa. *Assistant Director and Head of the Department of Research in Pure Chemistry.* (2, 1930)

Crider, Joseph O., M.D. Jefferson Medical College, Philadelphia, Pa. *Associate Professor of Physiology and Assistant Dean.* (1, 1935)

Crisler, George R., Ph.D., M.D. 33d Altitude Training Unit, Santa Ana Army Air Base, Santa Ana, Calif. *Captain, Medical Corps.* (1, 1930)

Crittenden, Phoebe J., M.S., Ph.D. Lawrence Climactic Laboratory, War Department, Lawrence, Mass. *Associate Physiologist.* (1, 1937; 3, 1937)

Cromwell, Hobart W., Sc.D. Abbott Laboratories, North Chicago, Ill. *Bacteriologist.* (6, 1929)

Crozier, William J., Ph.D. Biological Laboratories, Harvard University, Cambridge, Mass. *Professor of General Physiology.* (1, 1928)

Cruickschank, Ernest W. H., M.D., D.Sc., Ph.D. M.R.C.P., F.R.S.E. Marischal College, University of Aberdeen, Aberdeen, Scotland. *Professor of Physiology.* (1, 1931)

ɔnka, F. A., Ph.D. Bureau of Human Nutrition and Home Economics, U. S. Department of Agriculture, Beltsville, Md. *Senior Chemist.* (2, 1924)

Culler, Elmer A. K., Ph.D. University of Rochester, Rochester, N. Y. *Professor of Psychology and Director of the Laboratory.* (1, 1936)

Cunningham, Raymond W., M.S., Ph.D. Temple University School of Medicine, Philadelphia, Pa. *Assistant Professor of Pharmacology.* (3, 1941)

Cunningham, Robert Sydney, A.M., M.D., Sc.D. Albany Medical College, Albany, N. Y. *Professor of Anatomy and Dean.* (1, 1923)

Curnen, Edward C., M.D. Hospital of Rockefeller Institute, 66th St. and York Ave., New York City. *Assistant Resident Physician, Hospital of The Rockefeller Institute; Assistant, Rockefeller Institute; Lieut. (j.g.) M.C. V(S) U.S.N.R. on active duty.* (6, 1941)

Curtis, George Morris, M.A., Ph.D., M.D. Kinsman Hall, Ohio State University, Columbus. *Professor of Surgery; Chairman, Department of Research Surgery.* (1, 1933; 4, 1933)

Curtis, Howard J., M.A., Ph.D. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Assistant Professor of Physiology.* (1, 1940)

Cutler, Elliott C., M.D. Peter Bent Brigham Hospital, Boston, Mass. *Moseley Professor of Surgery, Harvard Medical School; Surgeon-in-Chief, Peter Bent Brigham Hospital.* (4, 1927)

Cutting, Reginald A., M.D., Ph.D. Georgetown University School of Medicine, 3900 Reservoir Road, N.W., Washington, D. C. *Professor of Physiology and Director of the Department.* (1, 1939)

Cutting, Windsor C., M.D. Stanford University School of Medicine, San Francisco, Calif. *Assistant Professor of Therapeutics.* (3, 1939)

Daft, Floyd Shelton, Ph.D. National Institute of Health, Washington, D. C. *Senior Biochemist.* (5, 1941)

Daggs, Ray Gilbert, Ph.D. 2821 Milton Ave., Dallas, Texas. *Lt. Col., Hdqtrs. 8th Service Command Surgeon's Office.* (1, 1939; 5, 1933)

Dakin, Henry D., D.Sc., LL.D., Ph.D., F.I.C., F.R.S. Scarborough-on-Hudson, N. Y. (2, 1906)

Dalton, Albert J., M.A., Ph.D. National Institute of Health, Bethesda, Md. *Cytologist.* (4, 1942)

Dam, Henrik. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. (5, 1943)

D'Amour, Fred E., M.S., Ph.D. 2311 S. Josephine St., Denver, Colo. *Associate Professor, Department of Zoology, University of Denver.* (1, 1934)

D'Amour, Marie C., Ph.D., M.D. Tulane University, School of Medicine, New Orleans, La. *Instructor in Pharmacology.* (1, 1934)

Daniels, Amy L., Ph.D. College Highway, Avon, Conn. *Retired.* (2, 1919; 5, 1933)

Danielson, Irvin S., Ph.D. Pearl River Apartments, Apt. 3H, Pearl River, N. Y. *Research Chemist.* (2, 1937)

Dann, W. J., Ph.D. Box 3205, Duke Hospital, Durham, N. C. *Associate Professor of Physiology.* (2, 1937; 5, 1938)

Darrow, Chester W., Ph.D. Institute for Juvenile Research, 907 S. Wolcott St., Chicago, Ill. *Research Psychologist, Institute for Juvenile Research; Associate in Physiology, University of Illinois College of Medicine.* (1, 1937)

Darrow, Daniel Cady, M.D. New Haven Hospital, New Haven, Conn. *Associate Professor of Pediatrics, Yale University.* (2, 1936)

Davenport, Horace Willard, B.Sc. (Oxon.) Ph.D. Dept. of Physiology, Harvard Medical School, 25 Shattuck St., Boston, Mass. *Instructor in Physiology.* (1, 1942)

David, Norman Austin, M.D. University of Oregon Medical School, Portland. *Professor of Pharmacology.* (3, 1934)

Davidsohn, Israel, M.D. Mount Sinai Hospital, 2750 W. 15th Place, Chicago, Ill. *Pathologist and Director of Laboratories, Mt. Sinai Hospital;*

Assistant Professor of Pathology, College of Medicine, University of Illinois. (4, 1939; 6, 1929)

Davis, Hallowell, M.D. Harvard Medical School, Boston, Mass. *Associate Professor of Physiology.* (1, 1925)

Davis, John Emerson, M.S., Ph.D. Dept. of Physiology and Pharmacology, Univ. of Arkansas School of Medicine, Little Rock. *Associate Professor of Pharmacology.* (1, 1941; 3, 1941)

Davson, Hugh, M.Sc., D.Sc. Dalhousie University, Halifax, N.S., Canada. Experimental Station, Porton, Wilts, England. *Associate Professor of Physiology.* (1, 1941)

Dawson, James Robertson, Jr., M.D. Vanderbilt Medical School, Nashville, Tenn. *Associate Professor.* (4, 1940)

Dawson, Martin H., M.D., C.M. Presbyterian Hospital, 620 W. 168th St., New York City. *Associate Professor of Medicine.* (4, 1934; 6, 1934)

Dawson, Percy M., M.D. 806 W. 31st St., Austin, Texas. (1, 1900)

Day, Harry G., D.Sc. University of Indiana, Bloomington. *Associate Professor, Dept. of Chemistry.* (5, 1940)

Day, Paul L., M.A., Ph.D. University of Arkansas School of Medicine, Little Rock. *Professor of Physiological Chemistry.* (2, 1934; 5, 1933)

DeEds, Floyd, M.A., Ph.D. Dept. of Pharmacology, Stanford University School of Medicine, San Francisco, Calif. *Principal Pharmacologist, U. S. Department of Agriculture, Bureau of Agricultural Chemistry and Industrial Chemistry.* (2, 1937; 3, 1927)

Defandorf, James Holmes, Ph.D. Office of the Chief of the Chemical Warfare Service, Washington, D. C. *Colonel, Sn.C.* (3, 1940)

de Gara, Paul F., M.D. 200 Pinehurst Ave., New York City. *Instructor in Pathology, Cornell University Medical College.* (6, 1941)

DeGraff, Arthur C., M.D. New York University College of Medicine, New York City. *Professor of Theraepeutics.* (3, 1937)

Deichmann, Wilhelm, M.Sc., Ph.D. 527 McAlpin, Cincinnati, O., *Instructor, Kettering Laboratory of Applied Physiology; Instructor in Physiology, University of Cincinnati, College of Medicine.* (3, 1941)

Dempsey, Edward W., Sc.M., Ph.D. Harvard Medical School, Boston, Mass. *Instructor in Physiology.* (1, 1940)

Derbyshire, Arthur J., Ph.D. Wayne University College of Medicine, Detroit, Mich. *Assistant Professor of Anatomy.* (1, 1939)

de Savitsch, Eugene, M.D. Suite 24, 1150 Connecticut Ave., Washington, D. C. *Consulting Surgeon, Glen Dale Sanatorium.* (4, 1934)

Deuel, Harry J., Jr., Ph.D. University of Southern California Medical School, Los Angeles. *Professor of Biochemistry.* (1, 1928; 2, 1924; 5, 1933)

Deulofeu, Venancio, D. Chem. Casilla Correo 2539, Buenos Aires, Argentina. *Professor of Organic Chemistry, University of Buenos Aires.* (2, 1942)

Dienes, Louis, M.D. Massachusetts General Hospital, Boston. *Bacteriologist.* (6, 1924)

Dill, David Bruce, M.A., Ph.D., Lt. Col., Q.M.C., 2033 Tempo. Bldg. A, Washington, D. C. *Assistant for Product Analysis, Research and Development Branch, OQMG.* (1, 1941; 2, 1927; 5, 1936)

Dille, James M., M.S., Ph.D. University of Illinois School of Medicine, 1853 Polk St., Chicago. (3, 1939)

Dillon, Robert T., M.S., Ph.D. % G. D. Searle and Co., Box 5110, Chicago 80, Ill. *Head, Analytical Division.* (2, 1934)

Dingle, John H., Sc.D., M.D. Thorndike Memorial Laboratory, Boston City Hospital, Boston, Mass. *Instructor and Francis Weld Peabody Fellow in Medicine, and Instructor in Bacteriology and Immunology, Harvard Medical School; Assistant Physician, Thorndike Memorial Laboratory; Assistant in Medicine, Boston City Hospital; Consultant to Secretary of War in Infectious Diseases.* (6, 1941)

DiPalma, Joseph R., M.D.* Kings County Hospital, Clarkson Ave., Brooklyn, N. Y. *Resident in Medicine.* (1, 1943)

Dixon, Harold M., M.D. University of Pennsylvania, Philadelphia. *Associate in Pathology; Chief of the Division of Pathology, Philadelphia General Hospital.* (4, 1936)

Doan, Charles A., M.D. Ohio State University, College of Medicine, Columbus. *Professor and Chairman of the Department of Medicine; Director of Medical Research.* (4, 1928)

Dochez, A. Raymond, M.D., Sc.D. (hon.). Presbyterian Hospital, 620 W. 168th St., New York City. *John E. Borne Professor of Medical and Surgical Research, Columbia University; Member of National Academy of Sciences.* (4, prior to 1920; 6, 1922)

Dohan, F. Curtis, M.D. 80 Princeton Rd., Cynwyd, Pa. *Fellow, George S. Cox Medical Research Institute; Associate in Medicine, University of Pennsylvania, Philadelphia.* (1, 1941)

Doisy, Edward A., M.S., Ph.D., Sc.D. St. Louis University School of Medicine, St. Louis 4, Mo. *Professor of Biological Chemistry; Member, National Academy of Sciences.* (2, 1920)

Dominguez, Rafael, M.D. Saint Luke's Hospital, 11311 Shaker Blvd., Cleveland, O. *Director of Laboratories, St. Luke's Hospital; Associate in Pathology, Western Reserve University.* (1, 1935)

Donahue, D. D., D.Sc. Division of Industrial Hygiene, National Institute of Health, Bethesda, Md. *Physiologist, Toxicology Section, Division of Industrial Hygiene, U. S. Public Health Service.* (3, 1941)

Dooley, M. S., M.D. 766 Irving Ave., Syracuse, N. Y. *Professor of Pharmacology, College of Medicine, Syracuse University.* (3, 1923)

Dorfman, Ralph I., Ph.D. Dept. of Biochemistry, Western Reserve University School of Medicine, Cleveland, O. *Assistant Professor of Biochemistry.* (2, 1940)

Dotti, Louis Basil, M.A., Ph.D. St. Luke's Hospital, Amsterdam Ave. and 113th St., New York City. *Chemist, St. Luke's Hospital; Associate in Physiology and Biochemistry, New York Medical College, Flower and Fifth Avenue Hospital, New York, N. Y.* (1, 1937)

Doty, J. Roy, Ph.D. American Dental Association Bureau of Chemistry, 222 E. Superior St., Chicago, Ill. *Associate Chemist.* (2, 1941)

Dow, Philip, Ph.D. University of Georgia School of Medicine, Augusta. *Associate Professor of Physiology.* (1, 1939)

Dow, Robert S., M.D., Ph.D. University of Oregon Medical School, Portland. *Associate Professor of Anatomy.* (1, 1940)

Downs, Ardrey W., M.A., M.D., D.Sc., F.A.C.P. University of Alberta, Edmonton, Canada. *Professor of Physiology and Pharmacology.* (1, 1917)

owns, Cora M., Ph.D. Department of Bacteriology, University of Kansas, Lawrence. *Professor of Bacteriology.* (6, 1929)

Drabkin, David L., M.D. Medical School, University of Pennsylvania, Philadelphia. *Associate Professor of Physiological Chemistry.* (2 1928; 5, 1934)

Dragstedt, Carl A., Ph.D., M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Professor of Pharmacology.* (1, 1928; 3, 1932)

Dragstedt, Lester R., M.D., Ph.D. University of Chicago, Chicago, Ill. *Professor of Surgery.* (1, 1920)

Draize, J. H., Ph.D. Division of Pharmacology, Food & Drug Administration, Federal Security Agency, Washington, D. C. *Pharmacologist.* (3, 1940)

Drake, T. G. H., M.B., F.R.C.P. (c). University of Toronto, Toronto, Canada. *Junior Demonstrator in Paediatrics, Department of Medicine, University of Toronto; Clinical Assistant on Active Staff and Associate Director Research Laboratory, Hospital for Sick Children.* (5, 1936)

Draper, William B., M.Sc., M.D. University of Colorado School of Medicine, 4200 E. 9th Ave., Denver. *Associate Professor of Physiology and Pharmacology.* (3, 1938)

Dresbach, Melvin, M.S., M.D. Hahnemann Medical College, Philadelphia, Pa. *Visiting Fellow in Physiology.* (1, 1912)

Dreyer, Nicholas Bernard, M.A. (Oxon). Long Island College of Medicine, 350 Henry St., Brooklyn, N. Y. *Associate Professor of Physiology and Pharmacology.* (3, 1942)

Drill, Victor Alexander,* Ph.D. Dept. of Pharmacology, College of Physicians and Surgeons, Columbia University, New York, N. Y. *Fellow of National Research Council.* (1, 1943)

Drinker, Cecil K., M.D. Harvard University School of Public Health, Boston, Mass. *Professor of Physiology and Dean.* (1, 1915)

Drinker, Katherine R., M.D. Harvard School of Public Health, 55 Shattuck St., Boston, Mass. *Instructor in Public Health.* (1, 1915)

Drury, Douglas R., M.D. University of Southern California, Los Angeles. *Professor of Physiology.* (1, 1932)

Dubin, Harry E., Ph.D. 250 E. 43rd St., New York City. *President, H. E. Dubin Laboratories, Inc.* (2, 1925)

DuBois, Eugene F., M.D. Cornell University Medical College, 1300 York Ave., New York City. *Professor and Head of the Department of Physiology and Biophysics; Attending Physician, New York Hospital; Member, National Academy of Sciences.* (1, 1913; 3, 1921; 5, 1935)

Dubos, Rene J., Ph.D., D.Sc. Harvard Medical School, Boston, Mass. *Professor of Tropical Medicine.* (6, 1938)

Dukes, H. H., D.V.M., M.S. New York State Veterinary College, Cornell University, Ithaca, N. Y. *Professor of Veterinary Physiology.* (1, 1934)

Dulaney, Anna D., A.M., Ph.D. Pathological Institute, University of Tennessee, Memphis. *Assistant Professor of Bacteriology, Medical School.* (6, 1924)

Dumke, Paul Rudolph, M.D. Department of Pharmacology, The Medical School, University of Pennsylvania, Philadelphia. *Instructor in Pharmacology.* (3, 1942)

Dunlap, Charles E., M.D. Tulane University of Louisiana, 1430 Tulane Ave. New Orleans. *Assistant Professor of Pathology.* (4, 1942)

Dunn, Max Shaw, Ph.D. University of California, Los Angeles. *Professor of Chemistry.* (2, 1933)

Durrant, Edwin Poe, M.A., Ph.D. Ohio State University, Columbus. *Associate Professor of Physiology.* (1, 1928)

Dutcher, R. Adams, M.S., M.A., D.Sc. Pennsylvania State College, State College. *Professor and Head of Department of Agricultural Biochemistry.* (2, 1920; 5, 1933)

Duval, Charles Warren, M.D. Tulane University, New Orleans, La. *Professor of Pathology and Bacteriology.* (4, prior to 1920)

du Vigneaud, Vincent, M.S., Ph.D. Cornell University Medical College, 1300 York Ave., New York 21, N.Y. *Professor of Biochemistry.* (2, 1929; 5, 1934)

Dworkin, Simon, D.D.S., M.D., C.M. Biology Building, McGill University, Montreal, Quebec, Canada. *Lecturer in Physiology, Faculty of Medicine.* (1, 1931)

Dye, J. A., Ph.D. James Law Hall, Cornell University, Ithaca, N. Y. *Associate Professor of Physiology.* (1, 1920)

Dye, Marie, M.S., Ph.D. Michigan State College, East Lansing. *Dean of Division of Home Economics.* (2, 1922; 5, 1933)

Dyer, Helen M., M.S., Ph.D. National Cancer Institute, U.S.P.H.S., Bethesda, Md. *Research Associate.* (2, 1936; 5, 1937)

Eadie, George S., Ph.D. Duke University School of Medicine, Box 3709, Durham, N. C. *Professor of Physiology and Pharmacology.* (1, 1929; 3, 1940)

Eagle, Harry, M.D. Johns Hopkins Hospital, Baltimore, Md. *Passed Assistant Surgeon, U. S. Public Health Service; Lecturer in Medicine, Johns Hopkins University Medical School.* (4, 1936)

Earle, Wilton R., Ph.D. U. S. Public Health Service, National Cancer Institute, Bethesda, Md. *Senior Cytologist.* (4, 1940)

Eaton, Alonzo Guy, M.A., Ph.D. Louisiana State University Medical Center, New Orleans. *Associate Professor of Physiology.* (1, 1933)

Eaton, Monroe D., M.D. State Department of Public Health, Influenza Laboratory, 1302 University Ave., Berkeley, Calif. *Staff Member, International Health Division of The Rockefeller Foundation.* (6, 1937)

Ecker, E. E., Ph.D. School of Medicine, Western Reserve University, 2085 Adelbert Rd., Cleveland, O. *Professor of Immunology.* (4, 1925)

Eckstein, Henry C., M.S., Ph.D. 320 W. Medical Building, University of Michigan, Ann Arbor. *Associate Professor of Biological Chemistry.* (2, 1925)

Eddy, Nathan B., M.D. National Institute of Health, Bethesda, Md. *Principal Pharmacologist, United States Public Health Service.* (1, 1919; 3, 1929)

Eddy, Walter H., A.M., Ph.D. 60 E. 42nd St., New York 18, N. Y. *Consultant; Professor Emeritus, Physiological Chemistry, Columbia University.* (2, 1913; 5, 1933)

Edsall, John Tileston, M.D. Harvard Medical School, Boston, Mass. *Associate Professor of Biological Chemistry and Tutor in Biochemical Sciences.* (2, 1931).

Edwards, Dayton J., Ph.D. 1300 York Ave., New York City. *Associate Professor of Physiology; Assistant Dean, Cornell University Medical College.* (1, 1921)

Edwards, Jesse E., M.D. 23 Edgehill Rd., Brookline, Mass. (4, 1911)

Edwards, J. Graham, A.M., Ph.D. 24 Hirl St., Buffalo, N. Y. *Assistant Professor of Anatomy, University of Buffalo.* (1, 1932)

Eggerth, Arnold H., Ph.D. Hygienic Laboratory, 535 Henry St., Brooklyn, N. Y. *Associate Professor of Bacteriology, Long Island College of Medicine.* (4, 1925)

Ehrenstein, Maximillian R., Ph.D. 806 Maloney Clinic, University of Pennsylvania Hospital, 36th and Spruce Sts., Philadelphia. *Assistant Professor of Chemistry, assigned to Medicine.* (2, 1942)

Eichelberger, Lillian, Ph.D. The Lasker Foundation for Medical Research, University of Chicago, Department of Medicine, Chicago, Ill. *Assistant Professor of Biochemistry.* (2, 1937)

Eisenman, Anna J., Ph.D. Yale University, New Haven, Conn. *Instructor, Department of Internal Medicine.* (2, 1930)

Elderfield, Robert C., Ph.D. Department of Chemistry, Columbia University, New York City. *Associate Professor.* (2, 1934)

Elftman, Herbert, M.A., Ph.D. College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City. *Instructor in Anatomy.* (1, 1940)

Eliot, Martha M., M.D. United States Children's Bureau, Washington, D. C. *Assistant Chief.* (5, 1933)

Elliott, K. Allan C., M.Sc., Ph.D. Institute of the Pennsylvania Hospital, 111 N. 49th St., Philadelphia. *Assistant Professor of Biochemistry in Psychiatry, University of Pennsylvania.* (2, 1937)

Ellis, Frederick W., M.D. Monson, Mass. (1, 1937)

Ellis, Lillian N., Ph.D. Adelphi College, Garden City, N. Y. (5, 1940)

Ellis, Max Mapes, A.M., Ph.D., Sc.D. University of Missouri, Columbia. *Professor of Physiology and Pharmacology.* (1, 1923)

Ellis, N. R., M.S. Bureau of Animal Industry, U. S. Department of Agriculture, Beltsville Research Center, Beltsville, Md. *Acting Chief, Animal Nutrition Division.* (2, 1925; 5, 1933)

Elser, William J., M.D. 1300 York Ave., New York City. *Emeritus Professor of Applied Pathology and Bacteriology, New York Hospital.* (6, 1920)

Elvehjem, Conrad Arnold, M.S., Ph.D., Sc.D. Biochemistry Building, University of Wisconsin, Madison. *Professor of Biochemistry; **Member**,*

National Academy of Sciences. (2, 1931; 5, 1933)

Emerson, George A., M.S., Ph.D. West Virginia School of Medicine, Morgantown. *Professor and Head, Department of Pharmacology.* (3, 1935)

Emerson, Gladys A., Ph.D. Merck Institute of Therapeutic Research, Rahway, N. J. *Nutritionist.* (5, 1942)

Emerson, Oliver H., Ph.D. Western Regional Research Laboratory, U. S. Dept. of Agriculture, Albany 6, Calif. *Assistant Chemist.* (2, 1938)

Emery, Frederick E., D.V.M., M.S., Ph.D. University of Buffalo Medical School, Buffalo, N. Y. *Assistant Professor of Physiology.* (1, 1930)

Emmett, Arthur D., M.A., Ph.D. Research Department, Parke, Davis & Co., Detroit, Mich. *Assistant Director of Research.* (2, 1908; 5, 1933)

Enders, John F., A.M., Ph.D. Department of Bacteriology, Medical School, Harvard University, Boston, Mass. *Assistant Professor of Bacteriology and Immunology.* (6, 1936)

Engle, Earl Theron, Ph.D. College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City. *Professor of Anatomy.* (1, 1930)

pstein, Albert A., M.D. 1111 Madison Ave., New York City. *Physician, Beth Israel Hospital; Physician, Hospital for Joint Diseases.* (2, 1912)

Erickson, Cyrus C., M.D. Duke University School of Medicine, Durham, N. C. *Associate in Pathology.* (4, 1941)

Erlanger, Joseph, M.D., LL.D., Sc.D. Washington University School of Medicine, 4580 Scott Ave., St. Louis, Mo. *Professor of Physiology; Member of the National Academy of Sciences.* (1, 1901)

Espe, Dwight L., Ph.D. Iowa State College, Ames. *Assistant Research Professor in Dairy Husbandry.* (1, 1940)

Essex, Hiram E., M.S., Ph.D. Mayo Foundation, Rochester, Minn. *Associate Professor of Physiology, Institute of Experimental Medicine.* (1, 1932; 3, 1940)

Ettinger, C. H., M.D., C.M., F.R.S.C.* Queen's University, Kingston, Canada. *Professor of Physiology.* (1, 1943)

Evans, Earl Alison, Jr., Ph.D. Department of Biochemistry, University of Chicago, Chicago, Ill. *Professor and Chairman of Department.* (2, 1939)

Evans, Everett Idris, M.D., Ph.D. Department of Surgery, Medical College of Virginia, Richmond. *Assistant Professor of Surgery; Responsible Investigator, Committee on Medical Research, National Research Council.* (1, 1935)

Evans, Gerald Taylor, M.D., Ph.D. University of Minnesota Hospitals, Minneapolis. *Director of Laboratory Service, University of Minnesota Hospitals; Associate Professor of Medicine, University of Minnesota.* (1, 1942)

Evans, Herbert M., M.D. University of California, Berkeley. *Professor of Anatomy and Director of Institute of Experimental Biology; Member of the National Academy of Sciences.* (1, 1919)

Evans, William E., Jr., M.S., Ph.D. University of Maryland Medical School, Baltimore. *Assistant Professor of Pharmacology.* (3, 1940)

Eveleth, D. F., Ph.D. University of Arkansas, Fayetteville. *Professor of Bacteriology and Veterinary Science.* (2, 1939)

Everett, Mark Reuben, Ph.D. University of Oklahoma Medical School, Oklahoma City. *Professor of Biochemistry.* (2, 1929)

Ewing, P. L., M.S., Ph.D. University of Texas School of Medicine, Galveston. *Associate in Pharmacology.* (3, 1938)

Eyster, John A. English, M.D. University of Wisconsin, Madison. *Professor of Physiology.* (1, 1906; 3, 1908)

Fahr, George, M.D. University of Minnesota Medical School, Minneapolis. *Professor of Clinical Medicine.* (1, 1913; 3, 1940)

Failey, Crawford F., Ph.D. 416 S. 6th St., Terre Haute, Ind. *Associate Professor of Pharmacology.* (2, 1933)

Fairhall, Lawrence T., M.A., Ph.D. U. S. Public Health Service, Washington, D. C. *Principal Industrial Toxicologist.* (2, 1924).

Falk, K. George, Ph.D. 40 E. 66th St., New York City. *Director, Laboratory of Industrial Hygiene.* (2, 1913)

Famulener, Lemuel W., Ph.C., M.D. Pathological Laboratory, St. Luke's Hospital, 113th St. and Amsterdam Ave., New York City. *Bacteriologist.* (6, 1920)

Farber, Sidney, M.D. Harvard Medical School, 25 Shattuck St., Boston, Mass. *Assistant Professor of Pathology.* (4, 1934)

Farmer, Chester J., A.M. Northwestern Medical School, 303 E. Chicago Ave., Chicago, Ill. *Professor of Chemistry.* (2, 1935)

Farr, Lee E., M.D. 2209 W. 11th St., Wilmington, Del. *Director of Research, Alfred I. duPont Institute.* During war: c/o C. P. Ritter, 800 Devon Ave., Los Angeles, Calif. (4, 1941)

Farrell, James I., Ph.D., M.D. 636 Church St., Evanston, Ill. (1, 1938)

Fassett, David W., M.D. Department of Therapeutics, New York University College of Medicine, 414 E. 26 St., New York City. *Fellow, Department of Therapeutics.* (3, 1942)

Fay, Marion, M.A., Ph.D. Woman's Medical College of Pennsylvania, East Falls, Phila-

delphia 29. *Professor of Physiological Chemistry.* (2, 1937)

Feldman, William H., D.V.M., M.S. Mayo Foundation, Rochester, Minn. *Associate in the Division of Experimental Surgery and Pathology.* (4, 1934)

Fellows, Edwin J., M.S., Ph.D. Temple University School of Medicine, Philadelphia, Pa. *Assistant Professor of Pharmacology.* (3, 1939)

Felton, Lloyd D., M.D., D.Sc. Division of Infectious Diseases, National Institute of Health, 25th and E Sts., N.W., Washington, D. C. *Senior Surgeon, United States Public Health Service.* (6, 1926)

Fenn, Wallace Osgood, A.M., Ph.D. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. *Professor of Physiology; Member, National Academy of Sciences.* (1, 1924)

Fenning, Con, M.D., M.A. University of Utah School of Medicine, Salt Lake City. *Associate Professor of Pharmacology and Physiology.* (1, 1942)

Ferguson, James Kenneth Wallace, M.A., M.D. 76 Kilbarry Rd., Toronto, Ontario, Canada. *Assistant Professor of Pharmacy and Pharmacology, University of Toronto, Toronto, Ontario, Canada.* (1, 1933; 3, 1941)

Ferguson, John Howard, M.D., M.A., L.M.S.S.A. University of Michigan, Ann Arbor. *Assistant Professor of Pharmacology.* (1, 1933; 3, 1939)

Ferguson, L. Kraeer, M.D. 133 S. 36th St. Philadelphia, Pa. *Assistant Professor of Surgery, University of Pennsylvania; Surgeon, Philadelphia General Hospital; Assistant Surgeon, University of Pennsylvania Hospital.* (4, 1935)

Ferry, John Douglass, Ph.D. Woods Hole Oceanographic Institution, Woods Hole, Mass. *Associate Chemist, U. S. Navy Antifouling Project, Woods Hole Oceanographic Institution; Research Associate, Harvard Medical School, Boston, Mass.* (2, 1941)

Ferry, Newell S., M.D. Parke, Davis & Co., Detroit, Mich. *Assistant Director of Research.* (6, 1916)

Ferry, Ronald M., M.D. 966 Memorial Drive, Cambridge, Mass. *Master of John Winthrop House.* (2, 1924)

Fevold, Harry L., M.S., Ph.D. Western Regional Research Laboratory, Albany 6, Calif. *Senior Biochemist.* (2, 1942)

Field, John, II, A.M., Ph.D. Stanford University, Stanford, Calif. *Professor of Physiology.* (1, 1930)

Fincke, Margaret L., Ph.D. Oregon State College, Corvallis. *Associate Professor of Foods and Nutrition, School of Home Economics.* (5, 1940)

Findley, Thomas, Jr., M.D. Ochsner Clinic, 3503 Prytania, New Orleans, La. *Head of the Department of Internal Medicine, Ochsner Clinic, New Orleans; Assistant Professor of Clinical Medicine, Tulane University School of Medicine.* (1, 1938)

Fine, Morris S., Ph.D. Central Laboratories, General Foods Corporation, Hoboken, N. J. *Director of Research.* (2, 1912; 5, 1933)

Finland, Maxwell, B.S. Boston City Hospital, Boston, Mass. *Assistant Professor of Medicine, Harvard Medical School.* (6, 1941)

Firor, Warfield Monroe, M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Surgery, Johns Hopkins University.* (1, 1932)

Fischer, Ernst, M.D., Dr. habil. Medical College of Virginia, Richmond. *Associate Professor of Physiology and Pharmacology.* (1, 1936)

Fischer, Hermann O. L., Ph.D. Banting Institute, 100 College St., University of Toronto, Toronto 5, Canada. *Research Professor of Organic Chemistry.* (2, 1940)

Fischer, Martin H., M.D., Pharm. D. (hon.), Sc.D. University of Cincinnati College of Medicine, Eden Ave., Cincinnati 19, O. *Professor of Physiology.* (1, 1901; 2, 1919)

Fishberg, Ella H., M.A., M.D. Beth Israel Hospital, Stuyvesant Park East, New York City. *Biochemist.* (2, 1931)

Fisher, Kenneth C., M.A., Ph.D. University of Toronto, Toronto, Ont., Canada. *Assistant Professor of Physiological Zoology.* (1, 1940)

Fiske, Cyrus H., M.D. Harvard Medical School, Boston, Mass. *Professor of Biological Chemistry.* (2, 1914)

Fitzgerald, Mabel P., 54 A, George Sq., Edinburgh, Scotland. (1, 1913)

Fitzhugh, O. Garth, Ph.D. Division of Pharmacology, Food and Drug Administration, Federal Security Agency, Washington, D. C. *Pharmacologist.* (3, 1940)

Fleischmann, Walter, M.D., Ph.D. Harriet Lane Home, Johns Hopkins Hospital, Baltimore, Md. *Associate in Pediatrics, Johns Hopkins University.* (1, 1940)

Fleisher, Moyer S., M.D. Jewish Hospital, St. Louis, Mo. *Research Bacteriologist.* (4, 1924; 6, 1932)

Flexner, Louis B., M.D. Department of Embryology, Carnegie Institution of Washington, Wolfe and Madison Sts., Baltimore, Md. *Research Associate.* (1, 1933)

Flock, Eunice V., Ph.D. Mayo Clinic, Rochester, Minn. *Assistant Professor of Biochemistry, University of Minnesota; Associate in the Division of Experimental Medicine, The Mayo Foundation.* (2, 1940)

Florman, Alfred L., M.D. 9th Service Command Laboratory, Presidio of Monterey, Calif. *Lieut., M. C.* (6, 1942)

Flosdorf, Earl W., Ph.D. 305 Lincoln Ave., Lansdowne, Pa. *Research—University of Pennsylvania School of Medicine.* (6, 1941)

Floyd, Cleveland, M.D., Sc.D. 246 Marlborough St., Boston, Mass. *Chief Examiner, Boston Health Dept.* (6, 1916)

Folch, Jordi, M.D. Rockefeller Institute for Medical Research, New York City. *Associate.* (2, 1941)

Follensby, Edna M., Ph.G. 80 E. Concord St., Boston, Mass. *Research Assistant, Evans Memorial.* (6, 1933)

Follis, Richard H., Jr., M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate in Pathology, The Johns Hopkins University.* (4, 1942)

Foot, Nathan Chandler, M.D. 340 E. 72nd St., New York City. *Professor of Surgical Pathology, Cornell University Medical College; Surgical Pathologist, New York Hospital.* (4, 1924)

Forbes, Alexander, A. M., M.D. Harvard Medical School, Boston, Mass. *Professor of Physiology; Member of the National Academy of Sciences.* (1, 1910)

Forbes, Ernest B., Ph.D. State College, Pa. *Director of the Institute of Animal Nutrition.* (1, 1917; 5, 1935)

orbes, Henry S., M.D. Forest St., Milton, Mass. *Associate in Neuropathology, Harvard Medical School.* (1, 1931)

Forbes, John C., M.A., Ph.D. Medical College of Virginia, Richmond. *Associate Professor of Biochemistry.* (2, 1937)

Forbes, William H., M.A., Ph.D.* Harvard University, Fatigue Laboratory, Boston, Mass. *Research Fellow, Assistant Director of Fatigue Lab., Assistant Professor of Industrial Physiology.* (1, 1943)

Foster, G. L., Ph.D. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Associate Professor of Biological Chemistry.* (2, 1923)

Foster, Harry E., M.D. Cutter Laboratory, Berkeley, Calif. *Medical Director.* (6, 1913)

Foster, Robert H. K., Ph.D., M.D. 160 Church St., Nutley, N. J. *Pharmacologist, Hoffman-La Roche, Inc.* (1, 1940)

Fothergill, LeRoy D., M.D. Naval Medical Center, Bethesda, Md. *Assistant Professor of Bacteriology and Immunology, Harvard Medical School. Now serving as Lt. Comdr. M. C., U. S. Naval Reserve.* (6, 1936)

Fraenkel-Conrat, Heinz, M.D., Ph.D. Western Regional Research Laboratory, Protein Division, Albany 6, Calif. *Associate Research Chemist.* (2, (1942)

Francis, Thomas, Jr., M.D., M.S., Sc.D. (hon.). School of Public Health, University of Michigan, Ann Arbor. *Professor of Epidemiology.* (4, 1940; 6, 1930)

Franke, Florent E., M.D. 9 Sylvester, Webster Groves, Mo. *Assistant Professor of Physiology, St. Louis University School of Medicine.* (1, 1934)

Frankel, Edward M., Ph.D. 214 River Rd., Nyack, N. Y. (2, 1916)

Fraser, Alexander MacLeod, A.M., M.D., C.M. McGill University, Montreal, Canada. *Lecturer in Pharmacology.* (3, 1939)

Fraser, Donald T., M.B. Connaught Laboratories, University of Toronto, Toronto 5, Canada. *Professor of Hygiene and Preventive Medicine.* (6, 1935)

Freeman, Harry, M.D. Worcester State Hospital, Worcester, Mass. *Internist, Research Service.* (1, 1939)

Freeman, Norman, E., M.D. University of Pennsylvania Medical School, Philadelphia. *J. Wm. White Assistant Professor of Research Surgery.* (1, 1936)

Freeman, Smith, M.D., Ph.D. Northwestern University School of Medicine, 303 E. Chicago Ave., Chicago, Ill. *Assistant Professor of Physiology and Pharmacology.* (1, 1937)

Freund, Jules, M.D. Bureau of Laboratories, Foot of E. 15th St., New York, N. Y. *Assistant Director.* (4, 1930; 6, 1924)

Friedgood, Harry B., M.D. Harvard Medical School, Boston, Mass. *Instructor in Medicine.* (1, 1936)

Friedemann, Theodore E., M.A., Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Associate Professor of Physiology.* (2, 1925)

Friedemann, Ulrich, M.D. Department of Bacteriology, The Jewish Hospital of Brooklyn, Classon and St. Marks Ave., Brooklyn, N. Y. (6, 1938)

Friedewald, William F., M.D. Internationa Health Division, The Rockefeller Foundation, 66th St. and York Ave., New York City. *Member of Staff.* (4, 1941)

Friedman, Maurice H., Ph.D., M.D. 2612 Tilden St., Washington, D. C. (1, 1929)

Friedman, M. H. F., M.A., Ph.D. Jefferson Medical College of Philadelphia, 1025 Walnut St., Philadelphia, Pa. *Assistant Professor of Physiology.* (1, 1941)

Friedman, Nathan B., M.D. Stanford University School of Medicine, San Francisco, Calif. *Instructor in Pathology.* Army Medical Museum, 7th & Independence, Washington, D. C. (4, 1942)

Frisch, Arthur W., Ph.D., M.D. College of Medicine, Wayne University, Detroit, Mich. *Instructor.* (6, 1938)

Fruton, J. S., Ph.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Associate in Chemistry.* (2, 1938)

Fulton, John Farquhar, M.A., Ph.D., M.D. Yale University School of Medicine, New Haven, Conn. *Sterling Professor of Physiology.* (1, 1925)

Funk, Casimir, D.Sc., Ph.D. 186 Riverside Drive, New York 24, N. Y. (2, 1921)

Furth, Jacob, M.D. Cornell University Medical College, 1300 York Ave., New York City. *Associate Professor of Pathology.* (4, 1932; 6, 1930)

Gaebler, Oliver H., Ph.D., M.D. Henry Ford Hospital, Detroit, Mich. *Associate in Chemistry.* (2, 1927)

Gaffron, Hans, Ph.D. Chemical Department, University of Chicago, Chicago, Ill. *Research Associate (Assistant Professor).* (2, 1941)

Gagge, Adolf Pharo, Ph.D. Aeromedical Research Laboratory, Wright Field, Dayton, O. *Major, Air Corps, U. S. Army; on leave from Yale University and John B. Pierce Laboratory of Hygiene.* (1, 1939)

Galambos, Robert, M.A., PhD. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. (1, 1942)

Gall, Edward A., M.D. Bethesda Hospital, Cincinnati, O. *Assistant Professor of Pathology, College of Medicine, University of Cincinnati.* (4, 1941)

Gallagher, Thomas F., Ph.D. University of Chicago, Chicago, Ill. *Associate Professor of Biochemistry.* (2, 1932)

Gallup, Willis D., M.S., Ph.D. Oklahoma Agricultural and Mechanical College, Stillwater. *Chemist and Professor of Agricultural Chemistry.* (2, 1932)

Gamble, James L., M.D., S.M. 33 Edgehill Rd., Brookline, Mass. *Professor of Pediatrics, Harvard Medical School.* (2, 1922; 5, 1933)

Gantt, W. Horsley, M.D. Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore, Md. *Associate in Psychiatry.* (1, 1935)

Garbat, Abraham L., M.D. 103 E. 78th St., New York City. *Attending Physician, Lenox Hill Hospital.* (6, 1913)

Gardner, Leroy U., M.D. Saranac Laboratory for Study of Tuberculosis, Saranac Lake, N. Y. *Director of the Trudeau Foundation.* (4, 1927)

Garrey, Walter Eugene, Ph.D., M.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Professor of Physiology.* (1, 1910; 2, 1906)

Gasser, Herbert S., A.M., M.D., Sc.D. (hon.) Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Director of Laboratories; Member of the National Academy of Sciences.* (1, 1915; 3, 1921)

Gates, Olive, M.D. 25 Shattuck St., Boston, Mass. *Associate Pathologist.* (4, 1940)

Gaunt, Robert, Ph.D. Washington Square College, New York University, New York City. *Assistant Professor of Biology.* (1, 1939)

Gay, Leslie N., M.D. 1114 St. Paul St., Baltimore, Md. *Director of the Allergy Clinic, Johns Hopkins Hospital; Visiting Physician to Johns Hopkins Hospital; Associate in Medicine, Johns Hopkins University.* (6, 1927)

Gelling, E. M. K., M.S., M.D., Ph.D. University of Chicago, Chicago, Ill. *Frank P. Hixon Distinguished Service Professor of Pharmacology and Chairman of Department.* (1, 1933; 2, 1927; 3, 1925)

Gelfan, Samuel, Ph.D. 51 W. Illinois St., Chicago, Ill. *Director of Research, Van Patten Pharmaceutical Co.* (1, 1930)

Gellhorn, Ernst, M.D., Ph.D. Room 116, Medical Sciences, University of Minnesota, Minneapolis. *Professor of Neurophysiology.* (1, 1930)

Gemmill, Chalmers L., M.D. School of Aviation Medicine, Pensacola, Fla. *Commander, U.S.N.R.* (1, 1928; 2, 1935)

Gerard, R. W., Ph.D., M.D. University of Chicago, Chicago, Ill. *Professor of Physiology.* (1, 1927)

Gerstenberger, Henry John, M.D. Western Reserve University, Cleveland, O. *Professor of Pediatrics, School of Medicine, Western Reserve University; Director of Pediatrics, Babies and Children's Hospital.* (5, 1938)

Gesell, Robert, M.D. University of Michigan, Ann Arbor. *Professor of Physiology.* (1, 1913)

Gettler, Alexander O., A.M., Ph.D., LL.D. 400 E. 29th St., New York City. *Professor of Chemistry and Toxicology, Washington Square College of New York University.* (2, 1916)

Gey, George Otto, M.D. Cancer Research and Tissue Culture Laboratory, Johns Hopkins Medical School, Baltimore, Md. *Instructor in Surgery.* (1, 1940)

Gibbs, Frederick Andrews, M.D. Neurological Unit, Boston City Hospital, Boston, Mass. *Instructor in Neurology, Harvard Medical School.* (1, 1935)

Gibbs, Owen Stanley, M.B., Ch.B. (Edin.) R.F.D. 4, Box 358-A, Memphis, Tenn. *Director, Medical Research Division, Plough, Inc.* (1, 1935; 3, 1930)

Gibson, Robert Banks, Ph.D. University Hospital, Iowa City, Iowa. *Associate Professor of Biochemistry, State University of Iowa.* (1, 1907; 2, 1906)

Gies, William John, M.S., Ph.D., Sc.D., LL.D., F.A.C.D. 632 W. 168th St., New York City.

Professor of Biological Chemistry, Columbia University. (1, 1898; 2, 1906; 3, 1909)

Gilbert, Ruth, A.M., M.D. R.F.D. 2, Altamont, N. Y. *Bacteriologist, New York State Department of Health, Albany.* (6, 1920)

Gilman, Alfred, Ph.D. 211 East Lake Ave., Baltimore 12, Md. (1, 1935; 3, 1934)

Gilson, Arthur S., Jr., A.M., Ph.D. Washington University Medical School, St. Louis, Mo. *Associate Professor of Physiology.* (1, 1927)

Githens, Thomas Stotesbury, M.D. The Cambridge, Wissahickon and Chelten Aves., Germantown, Philadelphia, Pa. (1, 1915)

Givens, Maurice H., Ph.D. 1750 N. Ashland Ave., Chicago, Ill. *Biochemist, Northwestern Yeast Company.* (1, 1917; 2, 1915)

Glaser, O. C., Ph.D. Amherst College, Amherst, Mass. *Professor of Biology.* (1, 1913)

Glazko, Anthony J., Ph.D. 2319 College Ave., Berkeley, Calif. *Naval Laboratory Research Unit No. 1, University of California, Berkeley.* (1, 1942)

Glick, David, Ph.D. Russell-Miller Milling Co. Minneapolis, Minn. *Head, Vitamin and Enzyme Research.* (2, 1936)

Goebel, Walther F., Ph.D. The Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Associate Member.* (2, 1929; 6, 1937)

Goerner, Alfred, Ph.G., Pharm. D., M.D. Long Island College of Medicine, 350 Henry St., Brooklyn, N. Y. *Associate Professor of Biological Chemistry.* (2, 1939)

Goettsch, Marianne, Ph.D. School of Tropical Medicine of Columbia University, San Juan, Puerto Rico. *Assistant Professor of Chemistry.* (2, 1933; 5, 1941)

Gold, Harry, M.D. 1300 York Ave., New York City. *Assistant Professor of Pharmacology, Cornell Medical College.* (3, 1927)

Goldblatt, Harry, M.D. Western Reserve University, Cleveland, O. *Professor of Experimental Pathology, and Associate Director, Institute of Pathology.* (4, 1927)

Goldfarb, Walter, M.D. 120 Station Hospital, A. P. O. 508, New York, N. Y. *Captain, M.C.* (1, 1938)

Goldforb, A. J., Ph.D. College of the City of New York, New York City. *Professor of Biology.* (1, 1930)

Goldring, William, M.D. New York University College of Medicine, 477 First Ave., New York City. *Assistant Professor of Medicine.* (1, 1939)

Goldschmidt, Samuel, Ph.D. University of Pennsylvania Medical School, Philadelphia. *Associate Professor of Physiology.* (1, 1919; 2, 1915)

Goldsmith, Grace A. Tulane University of Louisiana, New Orleans. (5, 1943)

Goodman, Louis Sanford, M.A., M.D. University of Vermont College of Medicine, Burlington. *Professor of Pharmacology and Physiology and Chairman of the Department.* (3, 1937)

Goodner, Kenneth, Ph.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Associate.* (6, 1932)

Goodpasture, Ernest William, M.D. Vanderbilt University Medical School, Nashville, Tenn. *Professor of Pathology,* (4, 1923)

Gordon, Albert S., M.S., Ph.D. Washington Square College of Arts and Sciences, New York University, New York City. *Instructor in Biology.* (1, 1942)

Gordon, Harry H., M.D. 525 E. 68th St., New York City. *Associate in Pediatrics, Cornell University Medical School; Associate Attending Pediatrician, New York Hospital; Medical Officer, U. S. Dept. Labor.* (5, 1940)

Gordon, William G., M.A., Ph.D. Eastern Regional Research Laboratory, U. S. Department of Agriculture, Chestnut Hill Station, Philadelphia, Pa. *Associate Chemist.* (2, 1939)

Goss, Harold, Ph.D. University of California College of Agriculture, Davis. *Associate Professor in Animal Husbandry.* (2, 1936; 5, 1933)

Gottschall, Russell Y., M.S., Ph.D. Bureau of Laboratories, Michigan Department of Health, Lansing. *Bacteriologist.* (6, 1939)

Goudsmit, Arnoldus, Jr., M.D., Ph.D. Doctors Hospital, 17th and Summer Sts., Philadelphia, Pa. *Director of Laboratories; Research Assistant, Philadelphia General Hospital, 1st Lieut. M.C., Station Hospital, Chanute Field, Rantoul, Ill.* (1, 1940)

Grabfield, G. Philip, M.D. The Longwood Medical Building, 319 Longwood Ave., Boston, Mass. *Associate in Medicine and Pharmacology, Harvard Medical School. (At present on leave of absence; Col. M. C., U. S. Army.)* (3, 1923)

Grady, Hugh G., M.D. Fitzgerald-Mercy Hospital, Darby, Pa. *Director of Laboratories.* (4, 1940)

Graef, Irving, M.D. New York University College of Medicine, New York City. *Associate Professor of Pathology; Pathologist, Bellevue Hospital and New York University Clinic.* (4, 1941)

Graham, Clarence H., Ph.D. Brown University, Providence, R. I. *Professor of Psychology.* (1, 1933)

Graham, Helen Tredway, A.M., Ph.D. Euclid Ave. and Kingshighway, St. Louis, Mo. *Associate Professor of Pharmacology, Washington University School of Medicine.* (1, 1933; 3, 1931)

Grant, R. Lorimer, M.S., Ph.D. Division of Pharmacology, Food and Drug Administration,

Federal Security Agency, Washington 25, D. C. *Pharmacologist.* (2, 1938)

Graubard, Mark, M.A., Ph.D. Department of Biology, Clark University, Worcester, Mass. *Research Associate.* (1, 1940)

Grauer, Robert C., M.D. Allegheny General Hospital, Pittsburgh, Pa. *Head of Department of Research in Endocrinology and Metabolism, William H. Singer Memorial Research Laboratory; Lecturer in Pathology, School of Medicine, University of Pittsburgh.* (4, 1941)

Graves, Stuart, M.D. School of Medicine, University of Alabama, University. *Dean and Professor of Pathology.* (6, 1918)

Gray, John S., M.S., Ph.D. Research Division, School of Aviation Medicine, Randolph Field, Texas. *Assistant Professor of Physiology, Northwestern University Medical School, Chicago, Ill. (on leave).* (1, 1937)

Gray, Samuel H., M.D. The Jewish Hospital of St. Louis, Kingshighway and Forest Park Blvd., St. Louis, Mo. *Pathologist, Jewish Hospital; Director of Laboratories, City Hospital; Associate Professor of Pathology, Washington University.* (4, 1939)

Greaves, J. D., M.S., Ph.D. Washington University School of Medicine, Scott and Euclid Aves., St. Louis, Mo. *Instructor in Biological Chemistry.* (2, 1938)

Greaves, Joseph E., Ph.D. Utah State Agricultural College, Logan. *Professor and Head of Department of Bacteriology and Biochemistry.* (2, 1940)

Greeley, Paul O., A.M., Ph.D., M.D. University of Southern California Medical School, University Park, Los Angeles. *Associate Professor of Medical Physiology.* (1, 1940)

Green, Arda A., M.D. School of Medicine, Washington University, St. Louis, Mo. *Research Associate in Pharmacology.* (2, 1932)

Green, Daniel, M.S., M.D. Camp Sutton Station Hospital, Charlotte Substation, Charlotte, N. C. *Instructor, Pharmacology and Therapeutics, University of Tennessee (on leave); Chief of the Medical Service, Camp Sutton Station Hospital, Charlotte Substation, U. S. Army.* (3, 1942)

Green, David E., Ph.D. Department of Medicine, College of Physicians and Surgeons, Columbia University, New York City. *Associate in Biochemistry.* (2, 1941)

Green, Harold David, M.D. Western Reserve University, School of Medicine, Cleveland, O. *Associate Professor of Physiology.* (1, 1936)

Green, Robert, M.A., M.D. 223 Millard Hall, University of Minnesota, Minneapolis. *Professor of Bacteriology and Immunology.* (6, 1930)

Greenberg, David Morris, Ph.D. University of California, Berkeley. *Professor of Biochemistry.* (2, 1927)

Greene, Carl Hartley, Ph.D., M.D. 401 Clinton Ave., Brooklyn, N. Y. *Associate Clinical Professor of Medicine, New York Post-Graduate Medical School of Columbia University; Clinical Professor of Medicine, Long Island College of Medicine.* (1, 1921; 2, 1922; 4, 1921)

Greene, Charles Wilson, A.M., Ph.D. 814 Virginia Ave., Columbia, Mo. *Lecturer in Physiology, Stanford University; Professor Emeritus of Physiology and Pharmacology, University of Missouri.* (1, 1900; 2, 1919; 3, 1909)

Greene, Harry S. N., M.D., C.M. Department of Pathology, Yale University School of Medicine, New Haven, Conn. *Professor of Pathology.* (4, 1937)

Greene, James Alexander, M.D. Baylor University, College of Medicine, Buffalo Drive., Houston, Texas. *Professor and Chairman of the Department of Internal Medicine and Dean of the Clinical Faculty.* (1, 1939)

Greene, Ronald R., M.S., M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Instructor in Physiology; Instructor in Obstetrics and Gynecology.* (1, 1941)

Greengard, Harry, Ph.D., M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Assistant Professor of Physiology.* (1, 1939)

Greenstein, Jesse P., Ph.D. National Cancer Institute, Bethesda, Md. *Senior Biochemist.* (2, 1935)

Greenwald, Isidor, Ph.D. 477 First Ave., New York City. *Associate Professor of Chemistry, New York University College of Medicine.* (2, 1912; 5, 1933)

Greep, Roy O., Ph.D. Squibb Institute for Medical Research, New Brunswick, N. J. *Research Associate in Pharmacology.* (1, 1940)

Greer, C. M., M.S. Vanderbilt University School of Medicine, Nashville, Tenn. *Research Associate in Pharmacology.* (3, 1938)

Gregersen, Magnus I., A.M., Ph.D. College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City. *Professor of Physiology.* (1, 1933)

Gregg, Donald Eaton, M.S., Ph.D. Department of Medicine, Western Reserve Medical School, 2109 Adelbert Rd., Cleveland, O. *Associate Professor of Physiology.* (1, 1933)

Greisheimer, Esther M., Ph.D., M.D. Division of Anesthesia, University of Minnesota, Minneapolis. *Assistant in Anesthesia.* (1, 1925)

Griffin, Angus, Ph.D. Department of Bacteriology, George Washington University School of Medicine, 1335 H St., N.W., Washington, D. C. *Assistant Professor of Bacteriology.* (6, 1940)

Griffith, Fred R., Jr., M.A., Ph.D. 24 High St., Buffalo, N. Y. *Professor of Physiology, Uni-*

versity of Buffalo Medical School. (1, 1923; 5, 1933)

Griffith, Wendell H., M.S., Ph.D. APO 871, New York, N. Y. *Lt. Col., Sanitary Corps, U. S. Army. On leave as Professor of Biological Chemistry, St. Louis University School of Medicine.* (2, 1923; 5, 1934)

Grimson, Keith S., M.D.* Duke University School of Medicine, Durham, N. C. *Associate Professor of Surgery.* (1, 1943)

Groat, William A., M.D. 713 E. Genesee St., Syracuse, N. Y. *Professor of Clinical Pathology, Syracuse University College of Medicine.* (6, 1917)

Grollman, Arthur, M.D., Ph.D. Dept. of Medicine, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C. *Research Professor of Medicine; Associate Professor of Physiology and Pharmacology.* (1, 1928; 3, 1933)

Gross, Erwin G., Ph.D., M.D. Medical Laboratories, State University of Iowa, Iowa City. *Professor of Pharmacology.* (1, 1927; 2, 1923; 3, 1927)

Gross, Robert E., M.D. Harvard Medical School, 300 Longwood Ave., Boston, Mass. *Assistant Professor of Surgery.* (4, 1940)

Gruber, Charles M., A.M., M.D., Ph.D. Jefferson Medical College, 1025 Walnut St., Philadelphia, Pa. *Professor of Pharmacology.* (1, 1914; 3, 1919)

Gruhzit, Oswald M., M.D. Research Laboratories, Parke, Davis & Co., Detroit, Mich. *Research in Pathology and Pharmacology.* (4, 1928)

undfest, Harry, A.M., Ph.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Assistant in Physiology.* (1, 1932)

Gudernatsch, F., Ph.D. Graduate School, New York University, Washington Square E., New York City. *Visiting Professor.* (1, 1930)

Guerrant, N. B., M.S., Ph.D. Pennsylvania State College, State College. *Professor of Biological Chemistry.* (2, 1934; 5, 1933)

Guest, George Martin, M.S., M.D. The Children's Hospital, Research Foundation, Elland and Bethesda Aves., Cincinnati, O. *Fellow of the Children's Hospital Research Foundation; Associate Professor of Pediatrics, University of Cincinnati, College of Medicine and Graduate School.* (2, 1933)

Gulick, Addison, A.M., Ph.D. 308 Westmount Ave., Columbia, Mo. *Professor of Physiological Chemistry, University of Missouri.* (1, 1915; 5, 1933)

Gunn, Francis D., M.D. Northwestern University School of Medicine, 303 E. Chicago Ave., Chicago, Ill. *Associate Professor of Pathology.* (4, 1938)

Gurin, S., M.S., Ph.D. University of Pennsylvania School of Medicine, Philadelphia. *Assistant Professor in Physiological Chemistry.* (2, 1938)

Gustavson, Reuben G., Ph.D. University of Colorado, Boulder. *Professor of Chemistry.* (2, 1927)

Gustus, Edwin L., M.Sc., Ph.D. 6505 Delaware St., Chevy Chase 15, Md. *Research and Development Branch, Military Planning Division, OQMG, War Department, Director of Research.* (2, 1934)

Guthrie, Charles Claude, M.D., Ph.D., Sc.D. University of Pittsburgh Medical School, Pittsburgh, Pa. *Professor of Physiology and Pharmacology.* (1, 1905; 3, 1909)

de Gutiérrez-Mahoney, C. G., M.D. 1032 Andalusia Ave., Coral Gables, Fla. *Associate Professor of Neurology, Vanderbilt Univ. School of Medicine, Nashville, Tenn., Lt. Col., M.C., AAF., Regional Station Hospital.* (1, 1940; 4, 1941)

György, Paul, M.D. Babies' and Children's Hospital, Western Reserve University, 2103 Adelbert Rd., Cleveland, O. *Associate Professor of Pediatrics.* (2, 1938; 5, 1939)

Haag, Harvey B., M.D. Medical College of Virginia, Richmond. *Professor of Pharmacology.* (3, 1934)

Haag, J. R., Ph.D. Oregon Agricultural Experiment Station, Corvallis. *Chemist.* (5, 1941)

Hadley, Philip Bardwell, Ph.D. Institute of Pathology, Western Pennsylvania Hospital, Pittsburgh. *Chief of Bacteriological Service and Research Bacteriologist.* (4, 1927)

Hafkesbring, H. Roberta, Ph.D. Woman's Medical College of Pennsylvania, East Falls, Philadelphia. *Associate Professor of Physiology.* (1, 1931)

Haggard, Howard W., M.D. 4 Hillhouse Ave., New Haven, Conn. *Director of the Laboratory of Applied Physiology, Yale University.* (1, 1919; 2, 1920)

Hahn, Paul F., Ph.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Assistant Professor of Biochemistry.* (4, 1939)

Haig, Charles, M.A., Ph.D. New York Medical College, Flower and Fifth Avenue Hospital, Fifth Ave. at 105th St., New York City. *Assistant Professor of Physiology.* (1, 1942)

Haist, Reginald E., M.A., M.D., Ph.D.* University of Toronto, Toronto, Ontario, Canada. *Assistant Professor of Physiology.* (1, 1943)

Haldi, John, A.M., Ph.D. Emory University, Emory University, Ga. (1, 1928)

Hale, Worth, M.D. Harvard Medical School, Boston, Mass. *Associate Professor of Pharmacology.* (1, 1908; 3, 1908)

Hale, Wm. M., M.D. The State University of Iowa College of Medicine, Iowa City. *Professor of Bacteriology.* (4, 1911; 6, 1935)

Hall, F. G., M.A., Ph.D. Duke University, Durham, N. C. *Professor of Zoology.* (1, 1937)

Hall, George Edward, M.D., Ph.D. Banting Institute, University of Toronto, Toronto, Canada. *Associate Professor.* (1, 1938)

Hall, Victor E., M.A., M.D. Department of Physiology, Stanford University, Calif. *Professor of Physiology.* (1, 1931)

Halliday, Nellie, Ph.D. Research Laboratory, Mt. Zion Hospital, San Francisco, Calif. (5, 1933)

Halpert, Béla, M.D. University of Oklahoma School of Medicine, Oklahoma City. *Director of Laboratories and Professor of Clinical Pathology.* (4, 1936)

Halsey, John T., M.D. P. O. Box 264, Waveland, Miss. *Professor Emeritus of Pharmacology, Tulane University of Louisiana.* (3, 1929)

Halstead, Ward C., M.A., Ph.D. Dept. of Medicine, University of Chicago, Chicago, Ill. *Assistant Professor Experimental Psychology, Division of Psychiatry.* (1, 1942)

Ham, Arthur W., M.D. University of Toronto, Toronto 5, Canada. *Associate Professor of Anatomy; in charge of Histology.* (4, 1939)

Hambourger, Walter E., Ph.D., M.D. G. D. Searle & Co. (Skokie, Ill.), P. O. Box 5110, Chicago, Ill. *Pharmacologist.* (3, 1934)

Hamilton, Bengt L. K., M.D., Sc.D. 826 E. 61st St., Chicago, Ill. (2, 1925)

Hamilton, James B., Ph.D. University of Missouri, Dept. of Anatomy, School of Medicine, Columbia. *Associate Professor of Anatomy.* (1, 1938)

Hamilton, Tom S., M.S., Ph.D. 551 Old Agricultural Building, Urbana, Ill. *Professor of Animal Nutrition, University of Illinois.* (2, 1937; 5, 1938)

Hamilton, W. F., Ph.D. University of Georgia School of Medicine, Augusta. *Professor of Physiology and Pharmacology.* (1, 1924)

Hammett, Frederick S., M.S., A.M., Ph.D. 493 Commercial St., Provincetown, Mass. *Scientific Director, Lankenau Hospital Research Institute, Philadelphia, Pa.* (1, 1920; 2, 1917)

Hampel, C. W., Ph.D. New York University College of Medicine, New York, N. Y. (1, 1936)

Handley, Carroll A., Ph.D. University of South Dakota, School of Medical Sciences, Vermillion. *Professor of Physiology and Pharmacology, and Acting Head of the Department.* (3, 1942)

Haney, Hance F., Ph.D., M.D. University of Oregon Medical School, Portland. *Professor of Physiology and Head of the Department.* (1, 1939)

Hanger, Franklin, M.D. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Associate Professor of Medicine, Columbia University.* (6, 1930)

Hanke, Martin E., Ph.D. University of Chicago, Chicago, Ill. *Associate Professor of Biochemistry.* (2, 1925)

Hanke, Milton Theo., Ph.D. 7550 S. Green St., Chicago, Ill. *Research Consultant, Biochemistry and Nutrition.* (2, 1919)

Hanks, John H., Ph.D. Culion, Palawan, Philippine Islands. (6, 1935)

Hansen, Arild E., M.D. University of Minnesota Medical School, Minneapolis. *Professor of Pediatrics.* (4, 1911; 5, 1912)

Hanzal, Ramon Francis, M.A., Ph.D. Institute of Pathology, Western Reserve University, Cleveland, O. *Assistant Professor of Pathological Chemistry.* (2, 1935)

Hanzlik, Paul J., A.M., M.D. School of Medicine, Stanford University, Sacramento and Webster Sts., San Francisco, Calif. *Professor of Pharmacology.* (1, 1912; 3, 1912)

Hardy, James Daniel, A.M., Ph.D. Russell Sage Institute of Pathology, 525 E. 68th St., New York City. *Research Associate.* (1, 1939)

Hardy, Mary, D.Sc. The Brearley School, 610 E. 83rd St., New York City. *Teacher of Science.* (1, 1933)

Hare, Kendrick, Ph.D. State University of Iowa, Iowa City. *Assistant Professor of Anatomy.* (1, 1938)

Harger, R. N., M.A., Ph.D. Indiana University School of Medicine, Indianapolis. *Professor of Biochemistry and Toxicology.* (2, 1938)

Harkins, Henry Nelson, M.S., Ph.D., M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Surgery, Johns Hopkins University Medical School.* (1, 1942)

Harmon, Paul M., A.M., Ph.D. Indiana University, Bloomington. *Professor of Physiology.* (1, 1930)

Harne, O. G. University of Maryland School of Medicine, Baltimore. *Associate Professor of Histology.* (1, 1935)

Harned, Ben King, M.S., Ph.D. Woman's Medical College of Pennsylvania, East Falls, Philadelphia. *Professor of Pharmacology.* (2, 1931; 3, 1941)

Harris, Albert H., 2nd, M.D. Loudenville, N. Y. (6, 1937)

Harris, Albert Sidney, Ph.D. Western Reserve University School of Medicine, Cleveland, O. *Assistant Professor of Physiology.* (1, 1939)

Harris, Milton, Ph.D. National Bureau of Standards, Washington, D. C. *Director of Research,*

Textile Foundation Research Associateship. (2, 1939)

Harris, Robert S. Massachusetts Institute of Technology, Cambridge. *Assistant Professor of Nutritional Biochemistry.* (5, 1941)

Harris, William H., M.D. Tulane University School of Medicine, New Orleans, La. *Assistant Professor of Pathology and Bacteriology.* (4, 1925)

Harrison, Frank, M.S., Ph.D. University of Tennessee College of Medicine, Memphis. *Assistant Professor in Anatomy.* (1, 1941)

Harrison, Ross Granville, M.D., Ph.D., Sc.D. Osborn Zoological Laboratory, New Haven, Conn. *Sterling Professor of Biology, Emeritus, Yale University; Chairman of the National Research Council; Member of the National Academy of Sciences.* (1, 1906)

Harrison, R. Wendell, M.S., Ph.D. Ricketts Laboratory, University of Chicago, Chicago, Ill. *Associate Professor of Bacteriology.* (6, 1934)

Harrop, George A., M.D. The Squibb Institute for Medical Research, New Brunswick, N. J. *Director.* (2, 1922)

Harrow, Benjamin, M.A., Ph.D. College of the City of New York, Convent Ave. and 139th St. *Professor of Chemistry.* (2, 1927)

Hart, E. B., B.S. Agricultural College, Madison, Wis. *Professor of Biochemistry, University of Wisconsin.* (2, 1910; 5, 1933)

Hartley, Geo., Jr., M.A., Ph.D., M.D. Boston University School of Medicine, 80 E. Concord St., Boston, Mass. *Assistant Professor of Pathology.* (4, 1941; 6, 1941)

artline, H. K., M.D. Johnson Foundation, University of Philadelphia, Philadelphia, Pa. *Assistant Professor of Biophysics.* (1, 1929)

Hartman, Carl G., A.M., Ph.D. Department of Zoology, University of Illinois, Urbana. *Professor of Zoology and Head of the Department; Member, National Academy of Sciences.* (1, 1921)

Hartman, Frank Alexander, A.M., Ph.D. Department of Physiology, Ohio State University, Columbus. *Professor of Physiology and Chairman of the Department.* (1, 1916)

Hartman, F. W., M.D. Henry Ford Hospital, Detroit, Mich. *Pathologist.* (4, 1927)

Hartmann, Alexis F., M.S., M.D. 500 S. Kingshighway, St. Louis, Mo. *Professor of Pediatrics, Washington University School of Medicine.* (2, 1932)

Harvey, E. Newton, Ph.D. Guyot Hall, Princeton, N. J. *Henry Fairfield Osborn Professor of Biology, Princeton University; Member, National Academy of Sciences.* (1, 1914; 2, 1916)

Hass, George, M.D. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor of Pathology.* (4, 1939)

Hastings, A. Baird, Ph.D., Sc.D. Harvard Medical School, Boston, Mass. *Hamilton Kuhn Professor of Biological Chemistry; Member, National Academy of Sciences.* (1, 1927, 2, 1921; 5, 1940)

Hatcher, Robert A., Ph.M., M.D., D.Sc. 32-24 154th St., Flushing, N. Y. *Professor of Pharmacology Emeritus, Cornell Univ. Med. College.* 1, 1904; 2, 1906; 3, 1908)

Haterius, Hans O., Ph.D. Wayne University College of Medicine, Detroit, Mich. *Professor of Physiology.* (1, 1936)

Hauck, Hazel M., Ph.D. Cornell University, Ithaca, N. Y. *Professor of Home Economics.* (5, 1941)

Hauge, Siegfred M., Ph.D. Purdue University Agricultural Experiment Station, Lafayette, Ind. *Research Associate in Biochemistry.* (5, 1933)

Haury, Victor G., M.D. Jefferson Medical College, Philadelphia, Pa. *Associate Professor of Pharmacology.* (3, 1939)

Haven, Frances L., M.A., Ph.D. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. *Associate in Biochemistry.* (2, 1941)

Hawk, Philip B., M.S., Ph.D. 48-14 33rd St., Long Island City, N. Y. *President, Food Research Laboratories, Inc.* (1, 1903; 2, 1906)

Hawkins, J. E., Jr., B.A. (Oxon), Ph.D.* Harvard Medical School, Boston, Mass. *Instructor in Physiology.* (1, 1943)

Hawkins, William Bruce, M.D. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. *Associate Professor of Pathology.* (4, 1933)

Hawley, Estelle E., Ph.D. Medical School, University of Rochester, Rochester, N. Y. *Research Fellow in Pediatrics.* (5, 1935)

Hayman, J. M., Jr., M.D. Lakeside Hospital, Cleveland, O. *Professor of Clinical Medicine and Therapeutics, Western Reserve University.* (1, 1928; 3, 1932)

Haynes, Florence W., M.A., Ph.D. Harvard Medical School, 25 Shattuck St., Boston, Mass. *Research Fellow in Medicine.* (1, 1937)

Haythorn, Samuel R., M.D. Allegheny General Hospital, 320 E. North Ave., Pittsburgh, Pa. *Director of William H. Singer Memorial Laboratory.* (4, 1925)

Haywood, Charlotte, A.M., Ph.D. Mount Holyoke College, South Hadley, Mass. *Professor of Physiology.* (1, 1939)

Hazen, Elizabeth L., M.A., Ph.D. New York State Department of Health Laboratories, 339 E. 25th St., New York City. *Senior Bacteriologist.* (6, 1931)

Heard, R. D. H., M.A., Ph.D. Dalhousie University, Halifax, Nova Scotia. *Assistant Professor of Biochemistry.* (2, 1938)

Hecht, Selig, Ph.D. Columbia University, New York City. *Professor of Biophysics.* (1, 1920)

Heft, Hattie L., Ph.D. Teachers College, Columbia University, New York City. *Assistant Professor of Physiological Chemistry.* (2, 1927)

Hegnauer, Albert H., Ph.D. Syracuse University, Syracuse, N. Y. *Assistant Professor of Physiology.* (1, 1937)

Heidelberger, Michael, Ph.D., M.A. 620 W. 168th St., New York City. *Associate Professor of Biological Chemistry, Columbia University; Chemist to the Medical Service, Presbyterian Hospital.* (2, 1927; 6, 1935)

Heilbrunn, Lewis Victor, Ph.D. University of Pennsylvania, Philadelphia. *Professor of Zoology.* (1, 1930)

Heim, J. William, Ph.D. Aero-Medical Laboratory, Army Air Forces, Wright Field, Dayton, O. *Senior Research Physiologist; Assistant in Physiology, Harvard School of Public Health.* (1, 1936)

Heinbecker, Peter, M.D. Washington University Medical School, St. Louis, Mo. *Associate Professor of Surgery.* (1, 1930)

Helff, O. M., M.S., Ph.D. New York University, University Heights, New York City. *Associate Professor of Biology.* (1, 1932)

Hellbaum, Arthur A., M.A., Ph.D. University of Oklahoma School of Medicine, Oklahoma City. *Assistant Professor of Physiology.* (1, 1937)

Hellebrandt, Frances Anna, M.D. Wisconsin General Hospital, Madison. *Research Associate in Physiology and Associate Professor of Physical Therapy, University of Wisconsin.* (1, 1933)

Heller, Victor G., Ph.D. Oklahoma A. & M. College, Stillwater. *Professor and Head of the Department of Agricultural Chemistry Research.* (2, 1935; 5, 1935)

Hellerman, Leslie, Ph.D. Johns Hopkins University School of Medicine, 710 N. Washington St., Baltimore, Md. *Associate in Physiological Chemistry.* (2, 1935)

Helmer, Oscar Marvin, M.S., Ph.D. Lilly Laboratory for Clinical Research, The Indianapolis City Hospital, Indianapolis, Ind. *Head of Department of Physiological Chemistry; Research Associate in the Department of Medicine, Indiana University School of Medicine.* (2, 1935)

Hemingway, Allan, Ph.D. 210 Millard Hall, University of Minnesota, Minneapolis. *Assistant Professor of Physiological Chemistry; Temporarily at School of Aviation Medicine, Randolph Field, Texas.* (1, 1933)

Henderson, Velyien E., M.A., M.B., F.R.S.C. Medical Bldg., University of Toronto, Toronto, Ont., Canada. *Professor of Pharmacology and Pharmacy.* (1, 1905; 3, 1911)

Henderson, Yandell, Ph.D., M.D. (hon.). 440 Prospect St., New Haven, Conn. *Professor of Physiology Emeritus, Yale University; Member, National Academy of Sciences.* (1, 1900; 2, 1919; 3, 1911)

Hendrix, Byron M., Ph.D. School of Medicine, University of Texas, Galveston. *Professor of Biochemistry.* (2, 1920)

Hendrix, James Paisley, M.A., M.D. Duke Hospital, Durham, N. C. *Associate in Medicine (in charge of Therapeutics); Associate in Physiology and Pharmacology, Duke University School of Medicine.* (3, 1942)

Hendry, Jessie L., M.A. Division of Laboratories and Research, New York State Department of Health, New Scotland Ave., Albany. *Senior Bacteriologist.* (6, 1938)

Henle, Werner, M.D. University of Pennsylvania, Philadelphia. *Assistant Professor of Bacteriology in Pediatrics.* (6, 1938)

Hepburn, Joseph Samuel, A.M., M.S., Ph.D., M.D. 235 N. 15th St., Philadelphia 2, Pa. *Professor of Chemistry and Research Associate in Gastro-Enterology, Hahnemann Medical College and Hospital.* (2, 1915)

Hepler, Opal, Ph.D., M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Assistant Professor of Pathology.* (4, 1939)

Herbst, R. M., Ph.D. Knollwood Road, Short Hills, N. J. *Assistant Professor of Organic Chemistry, New York University.* (2, 1938)

Herrick, C. Judson, Ph.D. 236 Morningside Drive, Grand Rapids, Mich. *Professor Emeritus of Neurology, University of Chicago; Member of the National Academy of Sciences.* (1, 1907)

Herrick, Julia F., M.A., Ph.D. Fort Monmouth, N. J. *Associate Physicist, Signal Service at Large; Assistant Professor of Biophysics, University of Minnesota; Associate in the Division of Experimental Medicine, Mayo Foundation (on leave).* (1, 1933)

Herrin, Raymond C., Ph.D., M.D. University of Wisconsin Medical School, Madison. *Associate Professor of Physiology.* (1, 1932)

Herrington, Lovic P., M.A., Ph.D. 290 Congress Ave., New Haven, Conn. *Associate Director, John B. Pierce Laboratory of Hygiene; Research Associate Professor, Dept. of Public Health, Yale Medical School.* (1, 1942)

Herriott, Roger M., Ph.D. Rockefeller Institute for Medical Research, Princeton, N. J. *Associate.* (2, 1940)

Herrmann, George, Ph.D., M.D. University of Texas, Medical Branch, Galveston. *Professor of Medicine.* (4, 1925)

Herrmann, Julian B., M.D. Yale School of Medicine, New Haven, Conn. *Research Assistant in Pharmacology.* (3, 1941)

Herrmann, Louis George, M.D. Cincinnati General Hospital, Cincinnati, O. *Associate Professor of Surgery, University of Cincinnati College of Medicine.* (4, 1933)

Hershey, A. D., Ph.D. Washington University School of Medicine, St. Louis, Mo. *Assistant Professor of Bacteriology and Immunology.* (6, 1942)

Hertig, Arthur T., M.D. Harvard University Medical School, 221 Longwood Ave., Boston, Mass. *Assistant Professor of Pathology and Assistant Professor of Obstetrics.* (4, 1941)

Hertz, Saul, M.D. Massachusetts General Hospital, Fruit St., Boston. *Research Associate, Harvard Medical School and Massachusetts Institute of Technology.* (4, 1935)

Hertzman, Alrick B., Ph.D. St. Louis University School of Medicine, St. Louis, Mo. *Professor of Physiology and Director of the Department.* (1, 1925)

Herwick, Robert P., Ph.D., M.D. U. S. Food and Drug Administration, Washington, D. C. *Senior Pharmacologist and Assistant Chief, Drug Division.* (3, 1938)

Hess, Charles L., M.S., M.D. 308 Davidson Bldg., Bay City, Mich. (1, 1916)

Hess, Walter C., Ph.D. Chemo-Medical Research Institute, Georgetown University, Washington, D. C. *Associate Research Professor.* (2, 1935)

Hetherington, Albert W., M.S., Ph.D.* Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Instructor in Neurology.* (1, 1943)

Hewitt, Earl Albon, M.S., Ph.D. Iowa State College, Ames. *Associate Professor of Veterinary Physiology.* (1, 1932)

Hewitt, Julia A. W., B.A. Nassau Hospital, Mineola, N. Y. *Senior Technician, in charge.* (6, 1921)

Heyroth, Francis F., M.D., Ph.D. Kettering Laboratory, College of Medicine, University of Cincinnati, Cincinnati, O. *Assistant Professor of Applied Physiology.* (2, 1935)

Hiatt, Edwin P., M.A., Ph.D. Vanderbilt University School of Medicine, Nashville, Tenn. *Instructor in Physiology.* (1, 1942)

Higgins, Harold Leonard, M.D. 322 Franklin, Newton, Mass. *Assistant Professor of Pediatrics, Harvard University.* (1, 1914; 5, 1933)

Hill, Edgar S., M.S., Ph.D. Washington University, College of Dentistry, St. Louis, Mo. *Associate Professor of Biological Chemistry and Physiology.* (2, 1936)

Hill, Robert M., M.S., Ph.D. 4200 E. 9th Ave., Denver, Colo. *Associate Professor of Biochemistry, University of Colorado Medical School.* (2, 1933)

Hill, Samuel E., M.A., Ph.D. Russell Sage College, Troy, N. Y. *Professor of Biology.* (1, 1934)

Hiller, Alma, Ph.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Associate.* (2, 1929)

Himmelsbach, C. K., M.D. U.S.P.H.S. Hospital, Lexington, Ky. *Passed Assistant Surgeon.* (3, 1938)

Himwich, Harold E., M.D. Albany Medical College, Albany, N. Y. *Professor of Physiology and Pharmacology.* (1, 1925; 5, 1933)

Hines, Harry M., M.S., Ph.D. The State University of Iowa, Iowa City. *Professor of Physiology.* (1, 1928)

Hines, Marion, Ph.D. Johns Hopkins Medical School, Baltimore, Md. *Associate Professor of Anatomy.* (1, 1932)

Hinrichs, Marie, Ph.D., M.D. Southern Illinois Normal University, Carbondale. *Associate Professor of Physiology; Head of Student Health Service.* (1, 1928)

Hinsey, Joseph C., M.S., Ph.D. Cornell University Medical College, 1300 York Ave., New York City. *Professor of Anatomy and Dean of the Medical College.* (1, 1929)

Hisaw, Frederick L., A.M., Ph.D. The Biological Laboratories, Harvard University, Cambridge Mass. *Professor of Zoology.* (1, 1932)

Hitchcock, David I., Ph.D. 333 Cedar St., New Haven, Conn. *Associate Professor of Physiology, Yale University.* (2, 1930)

Hitchcock, Fred A., M.Sc., Ph.D. Ohio State University, Columbus. *Associate Professor of Physiology.* (1, 1927; 5, 1933)

Hitchings, George H., M.S., Ph.D. 17 Priscilla Ave., Tuckahoe, N. Y. *Biochemist, Burroughs, Wellcome & Co.* (2, 1942)

Hjort, Axel M., M.D., Ph.D. 14 Fern Way (P. O. Box 281), Scarsdale, N. Y. *Private practice; research work at Grasslands Hospital.* (2, 1925)

Hoagland, Charles L., M.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Associate Member.* (6, 1940)

Hoagland, Hudson, M.S., Ph.D. Clark University, Worcester, Mass. *Professor of Physiology and Chairman of the Department of Biology.* (1, 1932)

Höber, Rudolf. University of Pennsylvania Medical School, Philadelphia. *Visiting Professor of Physiology.* (1, 1936)

Hodes, Robert, Ph.D. Johnson Foundation, University of Pennsylvania, Philadelphia. *Johnson Foundation Fellow in Medical Physics.* (1, 1941)

Hodge, Harold C., Ph.D. University of Rochester School of Medicine and Dentistry, Rochester,

N. Y. *Associate Professor of Biochemistry and Pharmacology.* (2, 1937)

Hoff, Ebbe Curtis, M.A., Ph.D. Department of Physiology, Yale University School of Medicine, 333 Cedar St., New Haven, Conn. (1, 1933)

Hoff, Hebbel E., M.A., Ph.D. McGill University, Montreal, Quebec, Canada. *Professor of Physiology.* (1, 1933)

Hoffman, Olive, M.S., Ph.D. Presbyterian Hospital, 51 N. 39th St., Philadelphia, Pa. (1, 1935)

Hoffman, William Samuel, Ph.D., M.D. 710 S. Wolcott Ave., Chicago, Ill. *Professor of Physiological Chemistry and Associate Professor of Medicine, Chicago Medical School.* (2, 1935)

Hogan, Albert G., A.M., Ph.D. 105 Schweitzer Hall, Columbia, Mo. *Professor of Animal Nutrition, University of Missouri.* (2, 1916; 5, 1933)

Hogness, Thorfin R., Ch.E., Ph.D. George Herbert Jones Chemical Laboratory, University of Chicago, Chicago, Ill. *Professor of Chemistry.* (2, 1941)

Holck, Harald G. O., Ph.D. College of Pharmacy, University of Nebraska, Lincoln. *Depts. of Physiology and Pharmacology, Associate Professor of Pharmacology.* (1, 1935; 3, 1938)

Hollander, Franklin, Ph.D. Mount Sinai Hospital, Fifth Ave. and 100th St., New York City. *Associate in Physiology; Head, Gastro-Enterology Research Laboratory.* (1, 1942; 2, 1932)

Holman, Russell Lowell, M.D. University of North Carolina School of Medicine, Chapel Hill. *Professor of Pathology.* (4, 1940)

Holmes, Arthur Dunham, Ph.D. Massachusetts State College, Amherst. *Research Professor of Chemistry.* (2, 1931; 5, 1933)

Holmes, Julia O., M.S., Ph.D. Massachusetts State College, Amherst. *Research Professor of Nutrition.* (2, 1942; 5, 1936)

Holt, Joseph Paynter, M.S., M.D., Ph.D. University of Louisville School of Medicine, 101 W. Chestnut St., Louisville, Ky. *Associate Professor of Physiology.* (1, 1942)

Holt, L. Emmett, Jr., M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Pediatrics, Johns Hopkins University.* (2, 1930)

Hoobler, Icie Macy, Ph.D. 660 Frederick St., Detroit, Mich. *Director of Research, Children's Fund of Michigan; Associate in Nutrition, Medical Staff of the Children's Hospital of Michigan.* (2, 1925; 5, 1933)

Hooker, Davenport, M.A., Ph.D. University of Pittsburgh School of Medicine, Pittsburgh, Pa. *Professor of Anatomy.* (1, 1920)

Hooker, Donald R., M.S., M.D. 19 W. Chase St., Baltimore, Md. *Lecturer in Physiological Hygiene, School of Hygiene and Public Health, Johns Hopkins University; Managing Editor of American Journal of Physiology, Physiological Reviews and Federation Proceedings.* (1, 1906; 3, 1911)

Hooker, Sanford B., A.M., M.D. 80 E. Concord St., Boston, Mass. *Member, Evans Memorial.* (6, 1918)

Hoppert, C. A., Ph.D. Michigan State College, Box 626, East Lansing. *Professor of Biological Chemistry.* (5, 1935)

Horsfall, Frank L., Jr., M.D., C.M. Rockefeller Institute, 66th St. and York Ave., New York City. *Member.* (6, 1937)

Horvath, Steven M., M.A., Ph.D.* Armored Forces Medical Research Laboratory, Ft. Knox, Ky. *Captain, San. Corps.* (1, 1943)

Horwitt, M. K., Ph.D. Biochemical Research Laboratory, Elgin State Hospital, Elgin, Ill. *Director, Biochemical Research Laboratory; Assistant Professor, Physiological Chemistry, University of Illinois School of Medicine.* (2, 1941)

Hoskins, R. G., Ph.D., M.D. Harvard Medical School, Boston, Mass. *Research Associate in Physiology, Harvard University; Director of Research, Memorial Foundation for Neuroendocrine Research.* (1, 1911)

Hotchkiss, Rollin D., Ph.D. The Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Associate.* (2, 1941)

Howard, Evelyn, A.M., Ph.D. Johns Hopkins School of Medicine, Baltimore, Md. *Instructor in Physiology.* (1, 1933)

Howard, Marion E., M.D. New Haven Hospital, New Haven, Conn. *Assistant Professor of Medicine, Yale School of Medicine; Associate Physician, New Haven Hospital and New Haven Dispensary.* (4, 1939; 6, 1937)

Howe, Paul E., A.M., Ph.D. 2823 29th St. N.W., Washington, D. C. *Colonel, Sanitary Corps; Chief, Nutrition Branch, Office of the Surgeon General, U. S. Army. On leave as Chief, Animal Nutrition Division, and Assistant Chief, Bureau of Animal Industry, U. S. Department of Agriculture.* (1, 1913; 2, 1909; 5, 1933)

Howe, Percy R., M.D., D.D.S. Harvard Medical School, Boston, Mass. *Director Forsyth Dental Infirmary; Professor Dental Sciences; Instructor in Pathology.* (5, 1935)

Howell, Katherine M., M.D. Michael Reese Hospital, 2900 Ellis Ave., Chicago, Ill. *Head of Departments of Bacteriology and Serology.* (6, 1940)

Howell, Stacey F., Ph.D. V. D. Research Laboratory, U. S. Marine Hospital, Stapleton, Staten Island, N. Y. *Chemist, U. S. Public Health Service.* (2, 1940)

Howell, William H., Ph.D., M.D., Sc.D., LL.D. 112 St. Dunstan's Road, Baltimore, Md. *Professor Emeritus of Physiology, Johns Hopkins*

University; Member, National Academy of Sciences. (1, 1887; 2, 1912)

Hubbard, Roger Sanford, A.M., Ph.D. 100 High St., Buffalo, N. Y. *Biochemist, Buffalo General Hospital; Professor of Applied Physiology, Buffalo University Medical School.* (1, 1922; 2, 1920)

Hubbell, Rebecca B., M.S., Ph.D. Connecticut Agricultural Experiment Station, New Haven. *Assistant Biochemist.* (2, 1937; 5, 1935)

Hudack, Stephen Sylvester, M.D. U. S. Naval Hospital, Brooklyn, N. Y. *Lt. Com.* (4, 1933)

Huddleston, Ora Leonard, M.D., Ph.D. University of Colorado School of Medicine, 4200 E. 9th Ave., Denver. *Instructor in Physiology.* (1, 1936)

Hueper, Wilhelm C., M.D. Warner Institute for Therapeutic Research, 113 W. 18th St., New York City. *Assistant Director and Principal Pathologist.* (4, 1940)

Huffman, C. F., M.S., Ph.D. Michigan State College, East Lansing. *Research Professor and Associate Professor in Dairy Husbandry.* (5, 1937)

Huggins, Charles Brenton, M.D. University of Chicago, Chicago, Ill. *Professor of Surgery.* (1, 1932)

Hughes, Joseph, M.D. 111 N. 49th St., Philadelphia, Pa. *Assistant Professor of Experimental Neurology, Graduate School of Medicine, University of Pennsylvania; Director of Laboratory, Pennsylvania Hospital for Mental Diseases.* (1, 1936)

Hughes, Josiah Simpson, M.A., M.S., Ph.D. Kansas State College, Manhattan. *Professor of Chemistry.* (2, 1931; 5, 1939)

Hughes, Thomas P., A.M., Ph.D. Rockefeller Foundation, 49 W. 49th St., New York City. *Member of Staff, International Health Division.* (6, 1934)

Hulpieu, Harold R., M.A., Ph.D. Indiana University School of Medicine, Indianapolis. *Associate Professor of Pharmacology.* (3, 1939)

Hunscher, Helen A., Ph.D. Western Reserve University, 2023 Adelbert Rd., Cleveland, O. *Head of Department of Home Economics.* (5, 1934)

Hunt, Reid, M.D., Ph.D., Sc.D. Harvard Medical School, Boston, Mass. *Professor Emeritus of Pharmacology, Harvard University; Member, National Academy of Sciences.* (1, 1895; 2, 1906; 3, 1908)

Hunter, Andrew, M.A., M.B., F.R.S.C. University of Toronto, Toronto, Canada. *Professor of Pathological Chemistry.* (2, 1908)

Hunter, George, M.A., D.Sc., F.R.S.C. University of Alberta, Edmonton, Canada. *Professor of Biochemistry.* (2, 1924)

Hunter, Jesse E., M.S., Ph.D. Allied Mills, Inc., 7500 S. Adams St., Peoria, Ill. *Director Biological Research.* (5, 1936)

Hussey, Raymond, M.D. Homewood Apartments, Baltimore, Md. (4, 1927)

Hyde, Roscoe R., A.M., Ph.D. Johns Hopkins University, Baltimore, Md. *Professor of Immunology.* (6, 1939)

Ingalls, Mabel S., Ph.D. 1218 Bank St., N. W., Washington 7, D. C. (6, 1940)

Ingle, Dwight J., M.S., Ph.D. The Upjohn Co., Research Department, Kalamazoo, Mich. *Upjohn Research Fellow.* (1, 1939)

Ingraham, Raymond Clifford, Ph.D. College of Medicine, University of Illinois, 1853 W. Polk St., Chicago. *Instructor in Physiology.* (1, 1938)

Ingram, W. R., Ph.D. College of Medicine, The State University of Iowa, Iowa City. *Professor and Head of the Department of Anatomy.* (1, 1936)

Irvin, J. Logan, Ph.D. Johns Hopkins University School of Medicine, 710 N. Washington St., Baltimore, Md. *Associate in Physiological Chemistry.* (2, 1942)

Irving, Laurence, A.M., Ph.D. Swarthmore College, Swarthmore, Pa. *Professor of Experimental Biology.* (1, 1927)

Irwin, Marian, Ph.D. The Rockefeller Institute for Medical Research, New York City. *Associate in the Division of General Physiology.* (1, 1927)

Irwin, M. R., Ph.D. Department of Genetics, University of Wisconsin, Madison. *Professor of Genetics.* (6, 1936)

Isaacs, Raphael, M.D. 104 S. Michigan Ave., Suite 408, Chicago 3, Ill. *Director, Department of Hematology, Michael Reese Hospital.* (4, 1928)

Isenberger, R. M., M.A., M.D. University of Kansas School of Medicine, Kansas City. *Professor of Pharmacology.* (3, 1937)

Ivy, Andrew C., Ph.D., M.D. 303 E. Chicago Ave., Chicago, Ill. *Nathan Smith Davis Professor of Physiology and Professor of Pharmacology, Northwestern University Medical School.* (1, 1919; 5, 1933)

Izquierdo, J. Joaquin, M.D. National School of Medicine, Mexico City. *Professor of Physiology in the National School of Medicine and the Escuela Medico Militar of Mexico.* (1, 1928)

Jackson, Dennis Emerson, A.M., Ph.D., M.D. University of Cincinnati Medical School, Eden and Bethesda Aves., Cincinnati, O. *Professor of Pharmacology.* (1, 1910; 3, 1912)

Jackson, Eugene L., Ph.D. Emory University, Ga. *Associate Professor of Pharmacology, Chairman, Department of Pharmacology.* (3, 1942)

Jackson, Richard W., Ph.D. Eastern Regional Research Laboratory, U. S. Department of

Agriculture, Wyndmoor, Pa. *Chief of Protein Division.* (2, 1930; 5, 1933)

Jacobs, Merkel Henry, Ph.D. University of Pennsylvania, Philadelphia. *Professor of General Physiology; Member of the National Academy of Sciences.* (1, 1919)

Jacobs, Walter A., A.M., Ph.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Member; Member, National Academy of Sciences.* (2, 1908; 3, 1913)

Jacobson, Edmund, Ph.D., M.D. Laboratory for Clinical Physiology, 310 S. Michigan Ave., Chicago, Ill. (1, 1929)

Jaffe, Henry L., M.D. Hospital for Joint Diseases, 1919 Madison Ave., New York City. *Director of Laboratories.* (4, 1925)

Jamieson, Walter A., Sc.D.(hon.). Eli Lilly & Company, Indianapolis, Ind. *Director, Biological Division.* (6, 1927)

Jaques, L. B., M.A., Ph.D.* University of Toronto, Toronto 5, Canada. *Lecturer and Research Associate, Dept. of Physiology.* (1, 1943)

Jasper, Herbert H., M.A., Ph.D., D. ès Sci. Montreal Neurological Institute, 3801 University St., Montreal, Que., Canada. *Lecturer in Neuroelectrography and Director of Department of Electrophysiology.* (1, 1940)

Jeans, P. C., M.D. State University of Iowa, Iowa City. *Professor of Pediatrics.* (5, 1937)

Jensen, H., Ph.D. Research Laboratories, The Upjohn Company, Kalamazoo, Mich. (2, 1929)

Jobling, James W., M.D. Columbia University, 630 W. 168th St., New York City. *Professor of Pathology.* (4—prior to 1920)

Jochim, Kenneth E., Ph.D. Michael Reese Hospital, 29th and Ellis Ave., Chicago, Ill. *Research Associate, Cardiovascular Dept.* (1, 1942)

Johlin, J. M., Ph.D., D.Sc. Vanderbilt University School of Medicine, Nashville, Tenn. *Associate Professor of Biochemistry.* (2, 1928)

Johnson, Charles C., M.D. University of Utah School of Medicine, Salt Lake City. *Professor of Pharmacology.* (3, 1929)

Johnson, Frank H., A.M., Ph.D. Princeton University, Princeton, N. J. *Assistant Professor, Dept. of Biology.* (1, 1942)

Johnson, Joseph L., Ph.D., M.D. School of Medicine, Howard University, Washington, D. C. *Professor and Head of the Department of Physiology.* (1, 1934)

Johnson, J. Raymond, Ph.D. Long Island College of Medicine, 350 Henry St., Brooklyn, N. Y. *Assistant Professor of Physiology and Pharmacology.* (1, 1938)

Johnson, Marvin J., M.S., Ph.D. University of Wisconsin, Madison. *Associate Professor of Biochemistry.* (2, 1941)

Johnson, Robert E., M.D., Ph.D. Fatigue Laboratory, Morgan Hall, Harvard University, Boston, Mass. *Research Fellow.* (2, 1939)

Johnson, Treat B., Ph.D. Amity Road, Bethany, Westville P. O., Conn. *Sterling Professor of Chemistry, Yale University; Member, National Academy of Sciences.* (2, 1910)

Johnson, Victor, Ph.D., M.D. 6807 Dorchester Ave., Chicago, Ill. *Associate Professor of Physiology; Dean of Students in the Division of Biology and the School of Medicine, University of Chicago.* (1, 1933)

Johnston, Charles G., M.S., M.D. Wayne University College of Medicine, Detroit, Mich. *Professor of Surgery.* (1, 1933)

Johnston, Margaret W., Ph.D. Box 276, Ann Arbor, Mich. *Research Associate in Internal Medicine.* (2, 1930; 5, 1938)

Jolliffe, Norman, M.D. 39 E. 75th St., New York, N. Y. (1, 1932)

Jones, D. Breese, Ph.D. Bureau of Human Nutrition and Home Economics, U. S. Department of Agriculture, Beltsville, Md. *Principal Chemist.* (2, 1920; 5, 1935)

Jones, James H., M.S., Ph.D. School of Medicine, University of Pennsylvania, Philadelphia. *Assistant Professor of Physiological Chemistry.* (2, 1928; 5, 1933)

Jones, Kenneth K., M.S., Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Associate Professor of Physiology and Pharmacology.* (1, 1936)

Jones, Lloyd R., M.S., Ph.D. 1402 S. Grand Blvd., St. Louis, Mo. *Associate Professor and Chairman of Department of Bacteriology, St. Louis University School of Medicine.* (6, 1933)

Joslin, Elliott P., M.A., M.D. New England Deaconess Hospital, 81 Bay State Rd., Boston, Mass. *Director, George F. Baker Clinic.* (5, 1933)

Jukes, Thomas Hughes, Ph.D. Lederle Laboratories, Pearl River, N. Y. *Associate Director, Pharmaceutical Division.* (2, 1935; 5, 1938)

Julianelle, Louis A., Ph.D., M.A. Division of Infectious Diseases, Public Health Research Institute of the City of New York, Foot of E. 15th St. *Head of Division.* (6, 1930)

Jung, Frederic Theodore, Ph.D., M.D. Northwestern University Medical School, Chicago, Ill. *Assistant Professor of Physiology and Pharmacology.* (1, 1930)

Jungeblut, Claus W., M.D. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Professor of Bacteriology, Columbia University.* (4, 1929; 6, 1926)

Kabat, Elvin A., Ph.D. The Neurological Institute, 710 W. 168th St., New York City. *Research Chemist.* (2, 1940)

Kabat, Herman, Ph.D., M.D. National Institute of Health, Bethesda, Md. *Pharmacologist.* (1, 1941)

Kahn, Reuben L., Sc.D. University of Michigan Hospital, Ann Arbor. *Director of Clinical Laboratories.* (4, 1934; 6, 1919)

Kalckar, Herman M., M.D., Ph.D. 439 W. 123rd St., New York City. *Research Associate.* (2, 1942)

Kamm, Oliver, M.S., Ph.D. Research Laboratory, Parke, Davis & Co., Detroit, Mich. *Scientific Director.* (2, 1928)

Karpovich, Peter V., M.D., M.P.E. School of Aviation Medicine, Randolph Field, Texas. *Senior Physiologist, Research Section.* (1, 1942)

Karr, Walter G., Ph.D. Smith, Kline & French Laboratories, Delaware Ave. & Poplar St., Philadelphia 23, Pa. *Director of the Research Laboratories; Assistant Professor of Physiological Chemistry, University of Pennsylvania; Consulting Biochemist to the Medical Clinic of the University Hospital, Bryn Mawr Hospital, Abington Memorial Hospital.* (2, 1925)

Karshan, Maxwell, Ph.D. Department of Biological Chemistry, Columbia University, 630 W. 168th St., New York City. *Associate Professor of Biochemistry.* (2, 1939)

Karsner, Howard T., M.D. Western Reserve University, 2085 Adelbert Rd., Cleveland, O. *Professor of Pathology; Director of the Institute of Pathology.* (4, prior to 1920; 6, 1925)

Katz, Gerhard, M.D. Tulane School of Medicine, New Orleans, La. *Assistant Professor of Pharmacology.* (3, 1937)

Katz, Louis Nelson, A.M., M.D. 2900 Ellis Ave., Chicago, Ill. *Director of Cardiovascular Research, Michael Reese Hospital; Professorial Lecturer in Physiology, University of Chicago.* (1, 1924)

Katzman, Philip A., Ph.D. St. Louis University School of Medicine, 1402 S. Grand Blvd., St. Louis 4, Mo. *Assistant Professor of Biochemistry.* (2, 1935)

Kay, H. D., Ph.D., D.Sc. National Institute for Research in Dairying, Shinfield, near Reading, England. *Director, Research Professor of Biochemistry, University of Reading.* (2, 1930)

Keeton, Robert W., M.S., M.D. University of Illinois College of Medicine, 1853 W. Polk St., Chicago. *Professor of Medicine.* (1, 1916; 3, 1924)

Kehoe, Robert A., M.D. Kettering Laboratory of Applied Physiology, College of Medicine, University of Cincinnati, Eden Ave., Cincinnati, O. *Research Professor of Physiology.* (1, 1940)

Keith, Norman M., M.D. Mayo Clinic, Rochester, Minn. *Consulting Physician, Division of Medicine, Mayo Clinic; Professor of Medicine, Mayo Foundation, University of Minnesota.* (1, 1920; 3, 1932; 4, 1924)

Keith, T. B., Ph.D. Pennsylvania State College, State College. *Assistant Professor of Animal Husbandry.* (5, 1941)

Keller, Allen D., Ph.D. Baylor University College of Medicine, Dallas, Texas. *Professor of Physiology and Pharmacology.* (1, 1931)

Kelser, Raymond A., Ph.D. 17 Oxford St., Chevy Chase, 15, Md. *Brig. General, U. S. Army.* (4, 1932)

Kelsey, F. Ellis, Ph.D. University of Chicago, Chicago, Ill. *Research Associate (Instructor) in Pharmacology.* (3, 1941)

Kempner, Walter, M.D. Duke University School of Medicine, Durham, N. C. *Assistant Professor of Medicine.* (1, 1940)

Kendall, Edward C., M.S., Ph.D., D.Sc. 627 Eighth Ave., S.W., Rochester, Minn. *Professor of Biochemistry, Mayo Foundation, University of Minnesota.* (1, 1916; 2, 1913; 4, prior to 1920)

Kennard, Margaret A., M.D. Psychiatric Division, Bellevue Hospital, First Ave. & 30th St., New York City. (1, 1934)

Kennedy, Cornelia, M.A., Ph.D. Snyder Hall, University Farm, St. Paul, Minn. *Associate Professor of Agricultural Biochemistry, University of Minnesota; Assistant Chemist, Minnesota Experiment Station.* (2, 1924; 5, 1934)

Kennedy, Robert P., M.D. Knollwood Drive, R. D. 1, Rochester, N. Y. (4, 1929)

Kenton, Harold B., Ph.D. New England Deaconess Hospital, Boston, Mass. *Bacteriologist and Director of the Blood Bank.* (6, 1934)

Kenyon, Allan T., M.D. University of Chicago, Division of Biological Sciences, 950 E. 59th St., Chicago, Ill. *Assistant Professor of Medicine.* 3, 1940)

Keresztesy, John C., M.A., Ph.D. Merck & Company, Inc., Rahway, N. J. *Head, Nutritional Research Laboratory.* (2, 1941)

Kerr, Stanley E., Ph.D. Near East College Association, 50 W. 50th St., New York City. *Professor of Biological Chemistry, American University of Beirut, Beirut, Syria, Republic of Lebanon.* (2, 1937)

Kerr, Wm. J., M.D. University of California Hospital, Third and Parnassus Aves., San Francisco. *Professor of Medicine, University of California; Physician-in-Chief, University of California Hospital.* (3, 1930)

Kesten, Homer D., M.D. College of Physicians and Surgeons, Columbia University, New York City. *Assistant Professor of Pathology.* (4, 1931)

Keys, Ancel, M.A., Ph.D., D. Phil. 51 Stadium South Tower, University of Minnesota, Minneapolis. *Professor of Physical Education and Physiology.* (1, 1939; 2, 1936)

Khorazo, Devorah, M.D. Apt. 4G, 480 W. 187th St., New York City. *Instructor in Bacteriology, Columbia University, Eye Institute.* (6, 1936)

Kidd, John G., M.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Associate Member in Pathology and Bacteriology.* (4, 1938; 6, 1937)

Kik, M. C., Ph.D. College of Agriculture, University of Arkansas, Fayetteville. *Assistant Professor of Agricultural Chemistry.* (5, 1912)

Kilborn, Leslie G., M.A., M.D., Ph.D. West China Union University, Chengtu, Szechwan, China. *Professor of Physiology and Pharmacology.* (1, 1928)

Killian, John Allen, A.M., Ph.D. Killian Research Laboratories, Inc., 49 W. 45th St., New York City. (2, 1921)

King, Barry G., M.A., Ph.D. College of Physicians and Surgeons, Columbia University, 630 West 168th St., New York City. *Assistant Professor of Physiology; Lieutenant, USNR, Naval Medical Research Institute, Bethesda, Md.* (1, 1938)

King, Charles Edwin, Ph.D. Vanderbilt University, Nashville, Tenn. *Associate Professor of Physiology.* (1, 1916)

King, Charles Glen, Ph.D. Nutrition Foundation, Inc., Chrysler Building, New York City. *Scientific Director.* (2, 1931; 5, 1933)

King, Jessie Luella, Ph.D. Goucher College, Baltimore, Md. *Professor of Physiology.* (1, 1914)

King, Joseph T., M.D., Ph.D. 314 Millard Hall, University of Minnesota Medical School, Minneapolis. *Assistant Professor of Physiology.* (1, 1931)

King, Lester, S., M.D. The Fairfield State Hospital, Newtown, Conn. *Hospital Pathologist.* (4, 1941)

Kirk, Paul L., Ph.D. University of California, Berkeley. *Associate Professor of Biochemistry.* (2, 1933)

Kirkbride, Mary B., Sc.D. Division of Laboratories and Research, New York State Department of Health, Albany. *Associate Director.* (6, 1921)

Kisch, Bruno, M.D.* 845 West End Ave., New York City. *Professor at Yeshiva College; In Charge of Experimental Medicine at Beth Israel Hospital.* (1, 1943)

Kleiber, M., D.Sc.* University of California, Davis. *Professor of Animal Husbandry.* (1, 1943; 5, 1933)

Klein, J. Raymond, Ph.D. University of Illinois, Neuropsychiatric Institute, 912 S. Wood St., Chicago. *Biochemist and Assistant Professor of Psychiatry and Physiological Chemistry.* (2, 1941)

Kleiner, Israel Simon, Ph.D. New York Medical College, Flower and Fifth Avenue Hospitals, New York 29, N. Y. *Professor of Physiology and Biochemistry.* (1, 1911; 2, 1912; 3, 1912; 5, 1933)

Kleitman, Nathaniel, A.M., Ph.D. University of Chicago, Chicago, Ill. *Associate Professor of Physiology.* (1, 1923)

Klemperer, Friedrich Wilhelm, M.D., Massachusetts General Hospital, Boston, Mass. *Assistant in Medicine.* (2, 1911)

Kletzien, Seymour W., M.S., Ph.D., 22 Lafayette Blvd., Williamsville, N. Y. *Biochemist.* (5, 1933)

Kline, O. L., Ph.D. U. S. Department of Agriculture, Food and Drug Administration, Washington, D. C. *Biochemist.* (5, 1936)

Klüver, Heinrich, Ph.D. University of Chicago, Chicago, Ill. *Member, Otho S. A. Sprague Memorial Institute.* (1, 1935)

Knoefel, Peter K., M.A., M.D. University of Louisville, Louisville, Ky. *Professor of Pharmacology.* (3, 1934)

Knowlton, Frank P., A.M., M.D. Syracuse University College of Medicine, Syracuse, N. Y. *Professor of Physiology.* (1, 1911)

Knowlton, G. Clinton, Ph.D. University of Iowa, Iowa City. *Assistant Professor of Physiology.* (1, 1938)

Knudson, Arthur, Ph.D. Albany Medical College, Albany, N. Y. *Professor of Biochemistry, Medical Department of Union University.* (2, 1919; 5, 1936)

Knutti, Ralph Eddy, M.D. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. *Assistant Professor of Pathology.* (4, 1933)

Kober, Philip A., B.S. Sherman Laboratories, Detroit, Mich. *Director of Research.* (2, 1912)

Koch, Elizabeth M., M.A., Ph.D. 1534 E. 59th St., Chicago, Ill. (2, 1925)

Koch, Fred Conrad, M.S., Ph.D. 1531 East 59th St., Chicago, Ill. *Director of Biochemical Research, Armour and Co.; Professor of Biochemistry Emeritus, University of Chicago.* (2, 1912; 5, 1933)

Kochakian, Charles D., A.M., Ph.D. University of Rochester Medical School, 260 Crittenden Blvd., Rochester, N. Y. *Research Associate, Dept. of Vital Economics.* (1, 1942)

Kocher, Rudolph Alfred, M.D. Box 926, Carmel, Calif. *Director, Velie Metabolic Clinic.* (2, 1915)

Koehler, Alfred E., M.D., Ph.D. 317 W. Pueblo St., Santa Barbara, Calif. *Physician, Sansum Clinic, Santa Barbara Cottage Hospital.* (2, 1924)

Koehne, Martha, Ph.D. Ohio State Department of Health, 75 Eighteenth Ave., Columbus. *Nutritionist.* (5, 1933)

Koepf, George F., M.D. Buffalo General Hospital, 100 High St., Buffalo, N. Y. *Instructor in Medicine, University of Buffalo.* (1, 1942)

Kohn, Henry I., Ph.D. Duke University School of Medicine, Durham, N. C. *Assistant Professor of Physiology and Pharmacology.* (1, 1940)

Kolmer, John A., M.S., M.D., D.P.H., Sc.D., LL.D., L.H.D. 1 Montgomery Ave., Bala-Cynwyd, Pa. *Professor of Medicine, Temple University; Director, Research Institute of Cutaneous Medicine.* (6, 1913)

Komarov, Simon A., M.S., M.D., Ph.D. S. S. Fels Fund, Med. Research Laboratory, 255 S. 17th St., Philadelphia, Pa. *Director of Dept. of Biochemistry.* (1, 1933)

Kopeloff, Nicholas, Ph.D. New York State Psychiatric Institute, 722 W. 168th St., New York City. *Principal Research Bacteriologist, New York State Psychiatric Institute and Hospital.* (6, 1937)

Koppanyi, Theodore, Ph.D. Georgetown University, Washington, D. C. *Professor of Pharmacology.* (1, 1924; 3, 1935)

Korr, Irwin M., M.A., Ph.D. 175 Pinckney Rd., Red Bank, N. J. *Physiologist, U. S. Signal Corps, Ft. Monmouth Signal Laboratories.* (1, 1939)

Kozelka, Frank L., Ph.D. Dept. of Pharmacology and Toxicology, University of Wisconsin, Madison. *Assistant Professor of Toxicology.* (3, 1939)

Krahl, Maurice E., Ph.D. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, Ind. *Research Biological Chemist.* (2, 1939)

Kramer, Benjamin, A.M., M.D. 6 Pierrepont St., Brooklyn, N. Y. *Pediatrician-in-Chief, Brooklyn Jewish Hospital; Professor of Clinical Pediatrics, Long Island College Medical School.* (1, 1915; 2, 1914)

Kramer, Martha, Ph.D. Department of Home Economics, Yenching University, Peiping, China. *Professor of Food Economics and Nutrition.* (5, 1933)

Krantz, John C., Jr., M.S., Ph.D. University of Maryland Medical School, Baltimore. *Professor of Pharmacology.* (3, 1937)

Krauss, William E., Ph.D. Ohio Experiment Station, Wooster. *Chief, Dairy Department.* (2, 1932; 5, 1933)

Kraybill, Henry R., M.S., Ph.D. 5720 Woodlawn Ave., Chicago 37, Ill. *Professorial Lecturer, Department of Biochemistry, University of Chicago; Director, Department of Scientific Research, American Meat Institute.* (2, 1942)

Krayer, Otto, M.D. Harvard Medical School, 25 Shattuck St., Boston, Mass. *Associate Professor of Comparative Pharmacology.* (3, 1938)

Krueger, Albert Paul, M.D. Captain M.C., U.S.N.R. 3517 Life Sciences Bldg., University of California, Berkeley. *Professor of Bacteriology; Officer in charge Lab. Research Unit No. 1, Berkeley, Calif.* (4, 1930; 6, 1937)

Krueger, Hugo M., Ph.D. St. Louis University Medical School, 1402 S. Grand Blvd., St. Louis, Mo. *Assistant Professor of Pharmacology.* (1, 1931; 3, 1935)

Krumbhaar, Edward B., M.D., Ph.D. University of Pennsylvania Medical School, Philadelphia. *Professor of Pathology.* (1, 1914; 4, prior to 1920)

Kruse, Harry Dayton, M.D., Sc.D. Milbank-Memorial Fund, 40 Wall St., New York City. (2, 1933)

Kruse, Theophile K., A.M., Ph.D. University of Pittsburgh Medical School, Pittsburgh, Pa. *Professor of Physiology and Pharmacology.* (1, 1919; 3, 1920)

Kubie, Lawrence S., M.D. 7 E. 81st St., New York City. *Associate in Neurology, College of Physicians and Surgeons, Columbia University; Associate Psychiatrist, Mt. Sinai Hospital, New York City.* (4, 1928)

Kuhn, Harry A., M.S. 524 Peabody St. N. W., Washington, D. C. *Colonel, C.W.S., War Department. Executive Officer, C. W. Procurement District.* (3, 1927)

Kuhn, Ludwig R., Ph.D. Department of Bacteriology, University of Georgia, Athens. *Associate Professor of Bacteriology and Immunology.* (6, 1939)

Kunde, Margarete M., Ph.D., M.D. 116 S. Michigan Ave., Chicago, Ill. *Instructor in Medicine, Northwestern University Medical School.* (1, 1924)

Kurtz, Alton C., Ph.D. Department of Biochemistry, Medical School, University of Oklahoma, Oklahoma City. *Assistant Professor.* (2, 1942)

Kydd, David M., M.D. Mary Imogene Bassett Hospital, Cooperstown, N. Y. *Associate Physician.* (5, 1934)

Kyes, Preston, A.M., Sc.D., M.D. North Jay, Me. (6, 1918)

Lacy, G. R., M.D. University of Pittsburgh, Pittsburgh, Pa. *Professor of Bacteriology and Immunology.* (4, 1927)

Lamb, Alvin R., M.S., Ph.D. Experiment Station, Hawaiian Sugar Planters' Association, Honolulu. *Research Associate.* (2, 1923; 5, 1934)

Lambert, Robert A., M.D. Rockefeller Foundation, 49 W. 49th St., New York City. *Associate Director for the Medical Sciences.* (4, 1922)

Lamport, Harold, M.D.* Yale University School of Medicine, New Haven, Conn. *Assistant Professor of Physiology.* (1, 1943)

Lamson, Paul Dudley, M.D. Vanderbilt University Medical School, Nashville, Tenn. *Professor of Pharmacology.* (1, 1921; 3, 1915)

Lamson, Robert W., A.M., Ph.D., M.D. Suite 810, 1930 Wilshire Blvd., Los Angeles, Calif. *Professor of Medicine and Public Health, University of Southern California School of Medicine.* (6, 1928)

Lancefield, Rebecca C., Ph.D. 4 Kenmore Rd., Douglaston, Long Island, N. Y. *Associate Member, Rockefeller Institute for Medical Research.* (6, 1933)

Landis, Carney, Ph.D. Psychiatric Institute and Hospital, Columbia University, 722 W. 168th St., New York City. *Principal Research Psychologist and Professor of Psychology.* (1, 1939)

Landis, Eugene Markley, Ph.D., M.D. Department of Physiology, Harvard Medical School, 25 Shattuck St., Boston, Mass. *George Higginson Professor of Physiology.* (1, 1928)

Lands, Alonzo M., M.A., Ph.D. Frederick Stearns and Co., 6533 Jefferson Ave., Detroit, Mich. *Research Assistant, Dept. of Physiology and Pharmacol.* (1, 1942)

Lange, Carl, M.D. 371 Morris St., Albany, N. Y. *Associate Bacteriologist, Divisions of Laboratories and Public Health, New York State Department of Health.* (6, 1938)

Langley, Wilson D., Ph.D. University of Buffalo Medical School, Buffalo, N. Y. *Associate Professor of Biological Chemistry.* (2, 1937)

Langworthy, Orthello R., M.A., M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Neurology, Johns Hopkins University.* (1, 1928)

Larrabee, Martin G., Ph.D. Johnson Foundation, Hospital of University of Pennsylvania, Philadelphia. *Fellow in Medical Physics and Lecturer in Biophysics.* (1, 1940)

Larson, Edward, Ph.D. Temple University Medical School, Broad and Ontario Sts., Philadelphia, Pa. *Associate Professor of Pharmacology.* (1, 1939; 3, 1937)

Larson, Hardy W., A.M., Ph.D. Metropolitan Life Insurance Co., Biochemical Laboratory, 1 Madison Ave., New York City. *Research Chemist.* (2, 1937)

Larson, Paul S., Ph.D. Medical College of Virginia, Richmond. *Associate in Physiology and Pharmacology.* (1, 1939)

Larson, W. P., M.D. University of Minnesota, Minneapolis. *Professor and Head of Department of Bacteriology and Immunology.* (6, 1917)

Lashley, Karl S., M.S., Ph.D. The Biological Laboratories, Harvard University, Cambridge, Mass. *Research Professor of Neuropsychology; Member of the National Academy of Sciences.* (1, 1923)

Laug, E. P., M.A., Ph.D. Division of Pharmacology, Food and Drug Administration, Federal Security Agency, Washington 25, D. C. *Pharmacologist.* (2, 1938)

Laurens, Henry, A.M., Ph.D., LL.D. School of Medicine, Tulane University, Station 20, New Orleans, La. *Professor of Physiology.* (1, 1913)

Lavine, T. F., Ph.D. Lankenau Hospital Research Institute, Philadelphia, Pa. *Research Chemist.* (2, 1938)

Lawson, Hampden, M.D., Ph.D. University of Louisville, Louisville, Ky. *Professor of Physiology.* (1, 1933)

Leake, Chauncey D., M.S., Ph.D. The University of Texas Medical Branch, Galveston. *Vice-President of the University of Texas in Charge of the Medical Program.* (1, 1923; 3, 1924)

Leathes, John Beresford, M.A., M.B., F.R.C.S., F.R.S. 106 Banbury Rd., Oxford, England. (2, 1909)

Lederer, Ludwig George, Ph.D., M.D. Pennsylvania Central Airlines, National Airport, Washington, D. C. *Assistant Chief, Medical Department.* (1, 1940)

Lederer, Max, M.D. 1037 President St., Brooklyn, N. Y. *Director of Laboratories, Jewish Hospital.* (6, 1920)

Lee, Milton O., M.A., Ph.D. Harvard Medical School, Boston, Mass. *Associate, Memorial Foundation for Neuro-endocrine Research; Research Fellow in Physiology.* (1, 1927; 5, 1933)

Lee, Robert C., B.Ch.E. Nutrition Laboratory, 20 Vila St., Boston, Mass. (5, 1940)

Leese, Chester E., M.S., Ph.D. George Washington University School of Medicine, Washington, D. C. *Associate Professor of Physiology.* (1, 1934)

Lehman, Arnold J., Ph.D., M.D. Wayne University College of Medicine, Detroit, Mich. *Assistant Professor of Pharmacology.* (3, 1937)

Lehman, Robert A., M.S., Ph.D. New York University College of Medicine, 477 First Ave., New York City. *Instructor in Therapeutics.* (3, 1942)

Lehmann, Gerhard, M.D., Dr. Ing. University of Louisville School of Medicine, Louisville, Ky. *Associate Professor of Pharmacology.* (3, 1939)

Lenhart, Carl H., M.D. Lakeside Hospital, 2065 Adelbert Rd., Cleveland, O. *Oliver H. Payne Professor of Surgery, Western Reserve University.* (1, 1921)

Lennette, Edwin H., Ph.D., M.D. Caixa Postal 49, Rio de Janeiro, Brazil. *Staff Member, International Health Division, The Rockefeller Foundation* (Mail at 49 W 49th St. New York City). (4, 1941)

Leonard, Clifford Shattuck, M.S., Ph.D. University of Vermont Medical College, Burlington. *Assistant Professor of Pharmacology.* (3, 1927)

Lepkovsky, Samuel, M.S., Ph.D. University of California, Berkeley. *Associate Professor of Poultry Husbandry.* (2, 1933; 5, 1933)

L'Esperance, Elise L., M.D. 321 E. 15th St., New York City. *Director of Laboratories, New York Infirmary for Women and Children.* (6, 1920)

Leverton, Ruth M., Ph.D. Department of Home Economics, University of Nebraska, Lincoln. *Associate Professor Human Nutrition Research.* (5, 1942)

Levin, Isaac, M.D. 57 W. Fifty-seventh St., New York City. *Clinical Professor of Cancer Research, New York University; Chief of the Department of Cancer Service, Montefiore Hospital; Director, New York City Cancer Institute.* (1, 1900)

Levin, Louis, Ph.D. Department of Anatomy, College of Physicians and Surgeons, Columbia University, New York City. *Research Associate in Anatomy.* (2, 1939)

Levine, Harold, Ph.D. Pabst Brewing Co., 917 W. Juneau Ave., Milwaukee, Wis. *Biochemist.* (2, 1933; 5, 1933)

Levine, Milton, M.S., Ph.D. Department of Bacteriology, Cook County Hospital, Chicago, Ill. (6, 1942)

Levine, Philip, M.D., M.A. Newark Beth Israel Hospital, 201 Lyons Ave., Newark, N. J. *Serologist and Bacteriologist.* (6, 1925)

Levine, Rachmiel, M.D., C.M. Michael Reese Hospital, Chicago, Ill. *Assistant Director, Dept. of Metabolism.* (1, 1942)

Levine, Samuel Z., M.D., New York Hospital, 525 E. 68th St., New York City. *Professor of Pediatrics, Cornell University Medical College; Pediatrician-in-Chief, New York Hospital.* (5, 1933)

Levine, Victor Emanuel, A.M., Ph.D., M.D. Creighton University School of Medicine, Omaha, Neb. *Professor of Biological Chemistry and Nutrition.* (2, 1936)

Levinson, Samuel A., M.D. University of Illinois College of Medicine, 808 S. Wood St., Chicago. *Professor of Pathology.* (4, 1938)

Levison, Louis A., M.D. 421 Michigan St., Toledo, O. *Physician to Toledo Hospital; Physician to St. Vincent Hospital.* (6, 1916)

Levy, Milton, Ph.D. 477 First Ave., New York City. *Assistant Professor of Chemistry, New York University College of Medicine.* (2, 1933)

Levy, Robert L., M.D. 730 Park Ave., New York City. *Professor of Clinical Medicine, College of Physicians and Surgeons, Columbia University.* (3, 1915)

Lewey, F. H., M.D. University Hospital, University of Pennsylvania, Philadelphia. *Visiting Professor of Neurophysiology and Consultant in Neurology.* (1, 1937)

Lewis, Howard Bishop, Ph.D. Medical School, University of Michigan, Ann Arbor. *Professor of Biological Chemistry and Director of the College of Pharmacy.* (1, 1925; 2, 1913; 5, 1933)

Lewis, Julian Herman, M.D. 4750 Champlain Ave., Chicago, Ill. *Associate Professor of Pathology, University of Chicago; Member of the Otho S. A. Sprague Memorial Institute.* (4, 1924)

Lewis, Robert C., Ph.D. 4200 E. 9th Ave., Denver, Colo. *Professor of Biochemistry, School of Medicine, University of Colorado.* (2, 1931; 5, 1933)

Lewis, Warren H., M.D. The Wistar Institute of Anatomy and Biology, Woodland Ave. and 36th St., Philadelphia, Pa. *Member; Member of the National Academy of Sciences.* (1, 1919)

Li, Richard D., M.D. Peiping Union Medical College, Peiping, China. *Instructor in Pharmacology.* (3, 1941)

Libby, Raymond L., M.S., Ph.D. American Cyanamid Co., 1937 W. Main St., Stamford, Conn. *Bio-physicist.* (6, 1938)

Libet, Benjamin, Ph.D. 111 N. 49th St., Philadelphia, Pa. Department of Physiology, University of Pennsylvania. *Instructor in Physiology.* (1, 1942)

Libman, Emanuel, M.D. 180 E. 64th St., New York City. *Consulting Physician, Mount Sinai Hospital.* (6, 1920)

Liddell, Howard S., A.M., Ph.D. Cornell University, Ithaca, N. Y. *Professor of Psychology.* (1, 1925)

Lieb, Charles C., M.D. 630 W. 168th St., New York City. *Hosack Professor of Pharmacology, College of Physicians and Surgeons, Columbia University.* (1, 1936; 3, 1915)

Lieberman, Arnold L., M.D., Ph.D. 738 Broadway, Suite 502, Gary, Ind. *Assistant in Medicine, Northwestern University.* (1, 1934)

Lightbody, Howard D., M.S., Ph.D. Western Regional Research Laboratory, U. S. Department of Agriculture, Albany 6, Calif. *Principal Biochemist.* (2, 1936)

Lillie, Ralph Stayner, Ph.D., Sc.D. University of Chicago, Chicago, Ill. *Professor Emeritus of General Physiology; Physiologist, Marine Biological Laboratory, Woods Hole, Mass.* (1, 1905; 2, 1913)

Lillie, R. D., M.D., Division of Pathology, National Institute of Health, Bethesda, Md. *Senior Surgeon, U.S.P.H.S.* (4, 1941)

Lim, Robert Kho-Seng, Ph.D., D.Sc., F.R.S.E. Peiping Union Medical College, Peiping, China. *Professor of Physiology, Director of Medical Relief Corps, China.* (1, 1923)

Lindsley, Donald B., M.A., Ph.D. Bradley Home, East Providence, R.I. *Director of Psychological and Neurophysiological Laboratory; Assistant Professor of Psychology, Brown University.* (1, 1937)

Linegar, Charles R., Ph.D. E. R. Squibb and Sons, Biological Laboratory, New Brunswick, N. J. *Chief, Biological Development and Control Laboratory.* (3, 1938)

Lineweaver, Hans, M.A., Ph.D. Western Regional Research Laboratory, U. S. Department of Agriculture, Albany 6, Calif. *Senior Biochemist.* (2, 1941)

Link, Karl Paul, Ph.D. Biochemistry Building, University of Wisconsin, Madison. *Professor of Biochemistry.* (2, 1931)

Lintz, William, M.D. 36 Plaza St., Brooklyn, N. Y. *Late Professor of Immunology and Bacteriology and Clinical Professor of Medicine, Long Island College of Medicine.* (6, 1920)

Lipman, Mrs. Miriam O., A.M. Presbyterian Hospital, 620 W. 168th St., New York City. *Research Assistant, Edward Daniels Faulkner Arthritis Clinic.* (6, 1931)

Lipmann, Fritz, M.D., Ph.D. Biochemical Research Laboratory, Massachusetts General Hospital, Boston. *Research Chemist; Head, Biochemical Research Laboratory.* (2, 1941)

Litchfield, John T., Jr., M.D. University of Minnesota Medical School, Minneapolis, 14. *Assistant Professor of Pharmacology.* (3, 1940)

Little, James Maxwell, M.S., Ph.D. Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C. *Assistant Professor of Physiology and Pharmacology.* (1, 1942)

Livingston, Alfred E., Ph.D. Temple University School of Medicine, Philadelphia, Pa. *Professor of Pharmacology.* (1, 1917; 3, 1920)

Lloyd, David P. C., D.Ph. Laboratory of Physiology, Yale University School of Medicine, 333 Cedar St., New Haven, Conn. *Assistant Professor of Physiology.* (1, 1939)

Locke, Arthur P., Ph.D. Institute of Pathology, Western Pennsylvania Hospital, Pittsburgh. *Research Biochemist.* (6, 1926)

Lodholz, Edward, M.D. Medical Laboratories, University of Pennsylvania, Philadelphia. *Isaac Ott Professor of Physiology, Graduate School of Medicine.* (1, 1913)

Loeb, Leo, M.D. Washington University Medical School, St. Louis, Mo. *Professor Emeritus of Pathology; Member, National Academy of Sciences.* (1, 1907; 4, prior to 1920)

Loebel, Robert O., M.D. Russell Sate Institute of Pathology, Cornell Medical College, 1300 York Ave., New York City. *Research Fellow; Adjunct Assistant Visiting Physician, Second (Cornell) Medical Division of Bellevue Hospital.* (1, 1928)

Loew, Earl R., M.S., Ph.D. Parke, Davis & Co., Detroit, Mich. (1, 1940)

Loewe, S., M.D. 17 Cole Terrace, New Rochelle, N. Y. *Hon. Prof. Pharmacology, Heidelberg; Dept. of Pharmacology, Cornell University Medical College.* (3, 1936)

Logan, Milan A., Ph.D. University of Cincinnati School of Medicine, Cincinnati, O. *Professor of Biological Chemistry.* (2, 1936)

Long, C. N. H., M.Sc., D.Sc., M.D. Yale University, New Haven, Conn. *Sterling Professor of Physiological Chemistry.* (1, 1935; 2, 1927)

Long, Esmond R., M.D. 7th and Lombard Sts., Philadelphia, Pa. *Director, Henry Phipps Institute; Professor of Pathology, University of Pennsylvania.* (4, 1930)

Long, Perrin Hamilton, M.D. The Johns Hopkins University, 615 N. Wolfe St., Baltimore, Md. *Professor of Preventive Medicine.* (3, 1940)

Longcope, Warfield T., M.D. Johns Hopkins Hospital, Baltimore, Md. *Professor of Medicine, Johns Hopkins University.* (3, 1921; 4, prior to 1920; 6, 1923)

Longenecker, Herbert Eugene, M.S., Ph.D. Department of Chemistry, University of Pittsburgh, Pittsburgh, Pa. *Professor of Chemistry and Director, Buhl Foundation Research Project.* (2, 1940)

Looney, Joseph Michael, M.D. Station Hospital, Fort Custer, Mich. *Chief of Special Service, Major, U. S. Army.* (2, 1922)

Loosli, Clayton Garr, M.D. The University of Chicago, Department of Medicine, Chicago, Ill. *Assistant Professor.* (4, 1940)

Lorente de Nó, Rafael, M.D. The Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member.* (1, 1937)

Lorenz, Egon, Ph.D. National Cancer Institute, Bethesda, Md. *Senior Biophysicist.* (4, 1942)

Loring, H. S., M.S., Ph.D. Stanford University, Calif. *Associate Professor of Biochemistry.* (2, 1938)

Lothrop, Alfred P., M.A., Ph.D. 279 Elm St., Oberlin, O. *Professor of Organic Chemistry, Oberlin College.* (2, 1912)

Loveless, Mary H., M.D. New York Hospital, 525 E. 68th St., New York City. *Research Associate, Cornell Medical School; Physician to Out-Patients, New York Hospital.* (6, 1941)

Lowell, Francis C., M.D. Nine Acre Corner, Concord, Mass. *Instructor in Medicine, Boston City Hospital.* (6, 1942)

Lowry, Oliver H., M.D., Ph.D. Research Laboratory, Public Health Research Institute of the City of New York, Foot of E. 15th St. *Research Associate.* (2, 1942)

Lubinski, Herbert, M.D. Jewish General Hospital, 3755 St. Catherine Rd., Montreal, Canada. *Bacteriologist.* (6, 1941)

Lucas, George H. W., M.A., Ph.D. University of Toronto, Toronto, Canada. *Associate Professor of Pharmacology.* (2, 1925; 3, 1928)

Luck, James Murray, Ph.D. Stanford University, Stanford, Calif. *Professor of Biochemistry.* (2, 1925)

Lucké, Balduin, M.D. 141 Montgomery Ave., Bala-Cynwyd, Pa. *Professor of Pathology, University of Pennsylvania Medical School.* (4, 1924)

Luckhardt, Arno Benedict, M.S., Ph.D., M.D. University of Chicago, Chicago, Ill. *Professor of Physiology.* (1, 1911)

Ludewig, Stephan, Ph.D. University of Virginia School of Medicine, University. *Assistant Professor of Biochemistry.* (2, 1941)

Luduena, Froilan P., Ph.D., M.D. Faculty of Medicine, Rosario, Argentina. *Professor Adjunto de Farmacologia.* (3, 1941)

Lukens, Francis D. W., M.D. University of Pennsylvania, 809 Maloney Clinic, 36th and Spruce Sts., Philadelphia. *Assistant Professor of Medicine and Director, George S. Cox Medical Research Institute.* (1, 1938)

Lund, E. J., Ph.D. Department of Zoology and Physiology, University of Texas, Austin. *Professor of General Physiology.* (1, 1930)

Lundgren, Harold P., Ph.D. Western Regional Research Laboratory, U.S.D.A., Albany 6, Calif. *Chemist.* (2, 1942)

Lundy, John Silas, M.D. The Mayo Foundation, Rochester, Minn. *Chief of Section on Anesthesia.* (3, 1935)

Lurie, Max B., M.D. Henry Phipps Institute, 7th and Lombard Sts., Philadelphia, Pa. *Assistant Professor of Experimental Pathology.* (4, 1934; 6, 1930)

Lutz, Brenton R., Ph.D. Boston University, 688 Boylston St., Boston, Mass. *Professor of Biology.* (1, 1925)

Luyet, Basile J., Sc.D. (Biol.), Sc.D. (Physics). St. Louis University School of Medicine, St. Louis, Mo. *Professor of Biology.* (1, 1936)

Lyall, Harold W., A.M., Ph.D. Division of Laboratories and Research, New York State Department of Health, Albany. *Assistant Director in charge of Antitoxin, Serum, and Vaccine Laboratories.* (6, 1937)

Lyman, Carl M., Ph.D. Division of Swine Husbandry, Agricultural Experiment Station, College Station, Texas. *Nutritionist.* (2, 1940)

Lyman, John F., Ph.D. Townshend Hall, Ohio State University, Columbus. *Professor of Agricultural Chemistry.* (2, 1920; 5, 1933)

Macallum, A. Bruce, M.D., Ph.D. Medical School, University of Western Ontario, London, Ont., Canada. *Professor of Biochemistry.* (2, 1914)

MacArthur, Edith H., A.M., Ph.D. Skidmore College, Saratoga Springs, N. Y. *Professor and Director of Home Economics.* (5, 1933)

MacCorquodale, D. W., M.S., Ph.D. Abbott Laboratories, North Chicago, Ill. *Head, Biochemical Research.* (2, 1934)

MacFadyen, Douglas A., M.A., M.D. Box 7, Room 103, Army Medical School, Army Medical Center, Washington, D. C. *Captain, U. S. Army.* (2, 1942)

MacKay, Eaton M., M.D. The Scripps Metabolic Clinic, La Jolla, Calif. (1, 1930)

Mackenzie, Cosmo G., D.Sc. The Johns Hopkins University, Baltimore, Md. *Associate in Biochemistry, School of Hygiene and Public Health.* (5, 1942)

Mackenzie, George M., M.D. Mary Imogene Bassett Hospital, Cooperstown, N. Y. *Physician-in-Chief; Director, Otsego County Laboratories.* (6, 1921)

MacLeod, Colin M., M.D. New York University College of Medicine, 477 First Ave., New York City. *Professor of Bacteriology.* (6, 1937)

MacLeod, Florence L., M.A., Ph.D. University of Tennessee, Knoxville. *Professor of Nutrition.* (2, 1927; 5, 1933)

MacLeod, Grace, M.A., Ph.D. 106 Morningside Drive, New York City. *Professor of Nutrition, Teachers College, Columbia University.* (2, 1924; 5, 1933)

MacLeod, John, M.S., Ph.D. Cornell University Medical College, 1300 York Ave., New York City. *Research Associate of Anatomy.* (1, 1942)

MacNeal, Ward J., M.D. New York Post-Graduate Medical School and Hospital, 303 E. 20th St., New York City. *Professor of Bacteriology.* (4, 1925)

MacNider, William deB., M.D., Sc.D., LL.D. University of North Carolina, Chapel Hill. *Kenan Research Professor of Pharmacology; Member, National Academy of Sciences.* (1, 1912; 2, 1912; 3, 1909; 4, prior to 1920)

Macht, David Israel, M.D., Phar. D. (hon.), Litt. D. Charles and Chase Sts., Baltimore, Md. *Director of Pharmacological Research Laboratory, Hynson, Westcott and Dunning, Inc.; Professorial Lecturer in Physiology, Yeshiva College, New York City.* (1, 1916)

Madden, Sidney C., M.D. University of Rochester School of Medicine and Dentistry, Rochester, N. Y. *Assistant Professor of Pathology.* (4, 1939)

Maddock, Stephen, M.D. Boston City Hospital, Boston, Mass. *Assistant in Surgery, Harvard Medical School; Director of Surgical Research Laboratory, City Hospital.* (4, 1931)

Madsen, Louis L., Ph.D. Bureau of Animal Industry, U. S. Department of Agriculture, Box 71, Berwyn, Md. *Nutritionist.* (5, 1940)

Maes, Julian P., M.D.* Dartmouth Medical School, Hanover, N. H. *Department of Pharmacology.* (1, 1943)

Magath, Thomas B., M.S., Ph.D., M.D. Mayo Clinic, Rochester, Minn. *Associate Professor of Clinical Bacteriology and Parasitology, University of Minnesota, Mayo Foundation; Consultant Physician in Clinical Laboratories, Mayo Clinic.* (1, 1928)

Magill, Thomas P., M.D. Cornell University Medical College, 1300 York Ave., New York City. (6, 1937)

Magoun, Horace W., Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Professor of Microscopic Anatomy.* (1, 1937)

Mahon, Eleanor Conway, Ph.D. Iron River, Mich. (4, 1940)

Main, Rolland J., Ph.D. Medical College of Virginia, Richmond. *Professor of Physiology.* (1, 1936)

Maison, George L., M.S., M.D. Aero-Medical Research Laboratory, Engineering Division, Wright Field, Dayton, O. *1st. Lt., Medical Corps., Assistant Professor of Physiology, Wayne University, Detroit, Mich.* (1, 1939)

Major, Randolph T., M.Sc., Ph.D. Cole Ave., Mountainside, Westfield, N. J. *Director of Research, Merck & Co.* (2, 1942)

Mallory, G. Kenneth, M.D. Mallory Institute of Pathology, Boston City Hospital, Boston, Mass. *Associate Professor.* (4, 1940)

Mallory, Tracy B., M.D. Massachusetts General Hospital, Boston. *Chief of Pathology and Bacteriology; Assistant Professor of Pathology, Harvard Medical School.* (4, 1937)

Maloney, Arnold H., Ph.D., M.D., LL.D. Howard University School of Medicine, Washington, D. C. *Professor and Head of Department of Pharmacology.* (3, 1932)

Maltaner, Frank, Ph.D. 388 New Scotland Ave., Albany, N. Y. *Associate Biochemist, Division of Laboratories and Research, New York State Department of Health.* (6, 1920)

Maluf, N. S. Rustum, M.S., Ph.D. Georgetown University Medical School, Washington, D. C. *Instructor in Physiology.* (1, 1942)

Man, Evelyn B., Ph.D. 333 Cedar St., New Haven, Conn. *Assistant Professor in the Biochemistry Laboratory, Yale University School of Medicine.* (2, 1936)

Manery, Jeanne Forest, M.A., Ph.D. Medical School, University of Toronto, Toronto, Ont., Canada. *Demonstrator in Biochemistry.* (1, 1937)

Mann, Frank C., M.A., M.D., Sc.D., LL.D. Mayo Clinic, Rochester, Minn. *Director, Division of Experimental Medicine; Professor of Experimental Medicine, Mayo Foundation.* (1, 1916; 3, 1923; 4, 1924)

Manville, Ira Albert, M.A., M.D., Ph.D. University of Oregon Medical School, Portland. *Associate Clinical Professor of Medicine and Director of Nutritional Research Laboratories.* (1, 1933)

Manwaring, Wilfred H., M.D. Stanford University, Palo Alto, Calif. *Professor Emeritus of Bacteriology and Experimental Pathology.* (4, prior to 1920; 6, 1917)

Marine, David, A.M., M.D. Montefiore Hospital, Gunhill Road and East 210th St., New York City. *Director of Laboratories.* (1, 1910; 4, prior to 1920)

Markowitz, J., M.D., Ph.D. 220 Bloor St., Toronto, Ont., Canada. *Research Associate in Physiology, University of Toronto, Faculty of Medicine.* (1, 1929)

Marmont, George H., Ph.D. Columbia University, 630 W. 168th St., New York City. *Research Associate in Physiology.* (1, 1941)

Marmorston, Jessie, M.D. 1165 Park Ave., New York City. (6, 1932)

Marrazzi, Amedeo S., M.D. Loyola University School of Medicine, Chicago, Ill. *Professor and Head of the Department of Pharmacology.* (3, 1938)

Marsh, M. Elizabeth, M.S., Ph.D. Killian Research Laboratories, 49 W. 45th St., New York City. *Assistant Director.* (1, 1929; 5, 1933)

Marshak, Alfred George, M.A., Ph.D. Radiation Laboratory, University of California, Berkeley. *Research Associate and Finney-Howell Fellow.* (1, 1940)

Marshall, Eli Kennerly, Jr., Ph.D., M.D., LL.D. Johns Hopkins Medical School, Baltimore, Md. *Professor of Pharmacology and Experimental Therapeutics; Member, National Academy of Sciences.* (1, 1915; 2, 1913; 3, 1915)

Marshall, Wade H., Ph.D. Wilmer Ophthalmological Institute, Johns Hopkins Hospital, Baltimore, Md. *Associate in Physiological Optics, Johns Hopkins University.* (1, 1937)

Martin, Donald Stover, M.D. Duke University School of Medicine, Duke Hospital, Durham, N. C. *Associate Professor of Bacteriology.* (4, 1940)

Martin, Stevens J., M.A., Ph.D. Tilton General Hospital, Fort Dix, N. J. *Capt. M. C., Chief of Sections on Anesthesia and Operating Pavilion, and Resuscitation and Oxygen Therapy.* (1, 1933)

Mason, Edward C., M.D., Ph.D. University of Oklahoma School of Medicine, Oklahoma City. *Professor of Physiology.* (1, 1935)

Mason, H. L., M.A., Ph.D. Mayo Clinic, Rochester, Minn. *Associate Professor of Physiological Chemistry, The Mayo Foundation, University of Minnesota.* (2, 1941)

Mason, Karl Ernest, Ph.D. The University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. *Professor of Anatomy.* (1, 1932; 5, 1941)

Mason, Morton F., Ph.D. Vanderbilt University Medical School, Nashville 4, Tenn. *Associate Professor of Biochemistry; Research Associate in Medicine.* (2, 1938)

Massengale, Oliver N., Ph.D. Mead Johnson & Co., Research Laboratory, Evansville, Ind. *Research Biochemist.* (2, 1937)

Mast, S. O., Ph.D. Johns Hopkins University, Baltimore, Md. *Professor of Zoology.* (1, 1920)

Mathews, Albert Prescott, Ph.D., D.Sc. (hon.). Woods Hole, Mass. *Professor Emeritus of Biochemistry, Univ. of Cincinnati.* (1, 1898; 2, 1906)

Mattill, Henry A., A.M., Ph.D. State University of Iowa, Iowa City. *Professor of Biochemistry.* (1, 1913; 2, 1909; 5, 1933)

Maurer, Frank W., Ph.D. Harvard School of Public Health, 55 Shattuck St., Boston, Mass. *Assistant Professor of Physiology.* (1, 1941)

Mavor, James Watt, Ph.D. Union College, Schenectady, N. Y. *Professor of Biology.* (1, 1930)

Mayerson, Hymen S., Ph.D. Tulane University School of Medicine, Station 20, New Orleans, La. *Associate Professor of Physiology.* (1, 1928)

Maynard, Leonard A., Ph.D. Cornell University, Ithaca, N. Y. *Professor of Animal Nutrition; Director of United States Soil, Plant and Nutrition Laboratory.* (2, 1930; 5, 1933)

McCann, William S., M.D., D.Sc. (hon.). University of Rochester, School of Medicine, Rochester, N. Y. *Dewey Professor of Medicine.* (2, 1923; 5, 1933)

McCarrell, June D., M.A., Ph.D. Dept. Surgica Research, Massachusetts General Hospital, Boston. *Research Fellow in Anesthesia, Massachusetts General Hospital; Instructor in Physiology, Harvard School of Public Health.* (1, 1942)

McCay, Clive M., M.S., Ph.D. Animal Nutrition Laboratory, Cornell University, Ithaca, N. Y. *Professor of Animal Nutrition.* (2, 1929; 5, 1933)

McClellan, Walter S., M.D. Saratoga Spa, Saratoga Springs, N. Y. *Medical Director; Associate Professor of Medicine, Albany Medical College.* (1, 1931)

McClendon, J. F., M.S., Ph.D. Route 1, Trooper Road, Norristown, Pa. *Research Professor of Physiology, Hahnemann Medical College.* (1, 1910; 2, 1914; 5, 1935)

McClosky, William T., B.A. 5120 7th St., N.W., Washington, D. C. *Senior Pharmacologist, Div. of Pharmacology, Food and Drug Administration, Federal Security Agency.* (3, 1929)

McCollum, Elmer Verner, M.A., Ph.D., Sc.D., LL.D. Johns Hopkins University, School of Hygiene and Public Health, 615 N. Wolfe St., Baltimore, Md. *Professor of Biochemistry; Member, National Academy of Sciences.* (2, 1910; 5, 1933)

McCouch, Grayson Prevost, M.D. University of Pennsylvania, Philadelphia. *Assistant Professor of Physiology.* (1, 1925)

McCrea, Forrest D., Ph.D. Duke University School of Medicine, Durham, N. C. *Associate Professor of Physiology and Pharmacology.* (1, 1929; 3, 1937)

McCrudden, F. H., M.D. 501 Boylston St., Boston, Mass. *Assistant Medical Director, New England Mutual Life Insurance Co.* (2, 1906)

McCullagh, D. Roy, M.Sc. (Man.); Ph.D. (Cantab.), FIC. 150 Northfield Rd., Bedford, O. *Vice-President.* (2, 1932)

McCulloch, Warren Sturgis, M.A., M.D. University of Illinois, College of Medicine, Chicago. *Associate Professor of Psychiatry.* (1, 1936)

McCutcheon, Morton, M.D. University of Pennsylvania Medical School, Philadelphia. *Professor of Pathology.* (4, 1925)

McDonald, Claude H., D.Sc. 5707 T St., Little Rock, Ark. *Head, Department of Physiology and Pharmacology, Arkansas University School of Medicine.* (1, 1936)

McDonald, Francis Guy, M.S., Ph.D. Research Laboratory, Mead Johnson & Co., Evansville, Ind. *Research Biochemist.* (2, 1936)

McEllroy, William Swindler, M.D. School of Medicine, University of Pittsburgh, Pittsburgh, Pa. *Professor of Physiological Chemistry; Dean, School of Medicine.* (2, 1919)

McFarland, Ross A.,* Ph.D. Harvard University, Division of Industrial Research, Graduate School of Business Administration, Soldiers Field, Boston, Mass. *Assistant Professor of Industrial Research.* (1, 1943)

McFarlane, William Douglas, Ph.D. Macdonald College, (McGill University), Macdonald College, P. Q., Canada. *Professor of Chemistry.* (2, 1933)

McGinty, Daniel A., M.A., Ph.D. Parke, Davis & Co., Detroit, Mich. *Research Physiologist.* (1, 1925)

McGuigan, Hugh Alister, Ph.D., M.D. 1853 W. Polk St., Chicago, Ill. *Professor of Pharmacology and Therapeutics, College of Medicine, University of Illinois.* (1, 1907; 2, 1906; 3, 1913)

McHargue, J. S., M.S., Ph.D., D.Sc. 411 Transylvania Park, Lexington, Ky. *Head, Department of Chemistry, Kentucky Agricultural Experiment Station.* (2, 1927)

McHenry, E. W., M.A., Ph.D., F.R.S.C. School of Hygiene, University of Toronto, Toronto, Canada. *Assistant Director, Connaught Laboratories; Associate Professor in Charge of Nutrition.* (2, 1938; 5, 1935)

McIntyre, A. R., Ph.D., M.D. College of Medicine, University of Nebraska, 42nd and Dewey Ave., Omaha. *Professor of Physiology and Pharmacology.* (1, 1933; 3, 1938)

McKee, Clara M., Squibb Institute for Medical Research, New Brunswick, N. J. *Assistant in Microbiology.* (6, 1941)

McLain, Paul L., M.D. University of Pittsburgh Medical School, Pittsburgh, Pa. *Assistant Professor of Physiology and Pharmacology.* (3, 1940)

McLean, Franklin C., Ph.D., M.D. University of Chicago, Chicago, Ill. *Professor of Pathological Physiology.* (1, 1914; 2, 1916; 3, 1916)

McLester, James S., M.D., LL.D. University of Alabama, 930 S. 20th St., Birmingham. *Professor of Medicine.* (5, 1933)

McMaster, Philip D., M.D. The Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. (4, 1921)

McMeekin, Thomas L., Ph.D. Eastern Regional Research Laboratory, U. S. Department of Agriculture, Philadelphia, Pa. *Senior Chemist.* (2, 1935)

MacNabb, Andrew L., V.S., B.V.Sc., F.A.P.H.A. Department of Health of Ontario, Toronto, Canada. *Director of Laboratories.* (6, 1941)

McNaught, James Bernard, M.D. Stanford University School of Medicine, San Francisco, Calif. *Associate Professor of Pathology.* (4, 1936)

McPhail, Murchie Kilburn, Ph.D. Dalhousie University, Halifax, Nova Scotia. *Professor of Pharmacology.* (3, 1941)

McQuarrie, Irvine, Ph.D., M.D. University of Minnesota, Minneapolis. *Professor and Head of Department of Pediatrics.* (4, 1927; 5, 1933)

Medes, Grace, Ph.D. Lankenau Hospital Research Institute, Philadelphia, Pa. *Research Physiological Chemist.* (2, 1930)

Medlar, Edgar M., M.D. Metropolitan Life Insurance Co. Sanatorium, Mt. McGregor, N. Y. *Pathologist.* (4, 1927)

Meek, Walter J., Ph.D. University of Wisconsin, Madison. *Professor of Physiology; Assistant Dean of the Medical School.* (1, 1908)

Mellon, Ralph R., M.D., M.Sc., Dr. P.H., Sc.D. (hon.). Institute of Pathology, Western Pennsylvania Hospital, Pittsburgh. *Director.* (6, 1918)

Melnick, Daniel, Ph.D. Food Research Laboratories, Inc., 48-14 33rd St., Long Island City, N. Y. *Chief Chemist.* (2, 1940; 5, 1942)

Melville, Kenneth Ivan, M.Sc., M.D., C.M. McGill University, Montreal, Canada. *Assistant Professor of Pharmacology.* (3, 1931)

Mendenhall, Walter L., S.M., M.D. Boston University Medical School, 80 E. Concord St., Boston, Mass. *Professor of Pharmacology.* (1, 1915; 3, 1917)

Menkin, Valy, M.A., M.D. Fearing Research Laboratory, Free Hospital for Women, 245 Pond Ave., Brookline, Mass. *Assistant Professor of Pathology.* (1, 1932; 4, 1932; 6, 1931)

Menten, Maud L., M.D., Ph.D. University of Pittsburgh, Pittsburgh, Pa. *Associate Professor of Pathology.* (1, 1915; 4, 1927)

Menzel, Arthur E. O., Ph.D. The Squibb Institute for Medical Research, New Brunswick, N. J. *Associate.* (6, 1939)

Mettler, Stacy R., M.D. University of California Hospital, San Francisco. *Associate Professor of Medicine.* (4, 1932)

Mettler, Fred A., A.M., Ph.D., M.D. Department of Neurology, College of Physicians and Surgeons, Columbia University, New York City. (1, 1937)

Meyer, Curtis E., M.S., Ph.D. The Upjohn Co., Kalamazoo, Mich. *Research Chemist.* (2, 1912)

Meyer, Karl, M.D., Ph.D. 630 W. 168th St., New York City. *Associate Professor of Biological Chemistry, College of Physicians and Surgeons, Columbia University.* (2, 1934)

Meyer, Karl F., M.D., Ph.D. Medical Center, San Francisco, Calif. *Professor of Bacteriology, University of California. Director of the George Williams Hooper Foundation for Medical Research.* (4, 1930; 6, 1922)

Meyerhof, Otto, M.D., LL.D. Department of Physiological Chemistry, University of Pennsylvania School of Medicine, Philadelphia. *Research Professor of Biochemistry.* (2, 1941)

Michaelis, Leonor, M.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member Emeritus.* (2, 1929)

Mider, George Burroughs, M.D. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor of Pathology.* (4, 1940)

Miles, Walter R., A.M., Ph.D. 333 Cedar St., New Haven, Conn. *Professor of Psychology, The School of Medicine and the Institute of Human Relations, Yale University; Member of the National Academy of Sciences.* (1, 1919)

Milhorat, Ade T., M.D. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor of Medicine and Instructor in Pharmacology; Research Fellow, Russell Sage Institute of Pathology.* (1, 1934; 3, 1937; 5, 1935)

Miller, B. F., Ch.E., M.D. University of Chicago, Chicago, Ill. *Assistant Professor of Medicine.* (2, 1938)

Miller, Carey D., University of Hawaii, Honolulu. *Professor of Food and Nutrition, Hawaii Agricultural Experimental Station.* (5, 1942)

Miller, C. Phillip, M.D., M.S. University of Chicago, Chicago, Ill. *Professor of Medicine.* (4, 1925; 6, 1928)

Miller, Edgar C. L., M.D. %Library, Medical College of Virginia, Richmond. *Directing Librarian.* (6, 1913)

Miller, Edgar G., Jr., Ph.D. 630 W. 168th St., New York City. *Professor of Biological Chemistry, Columbia University.* (2, 1930)

Miller, Franklin R., M.D. Jefferson Medical College and Hospital, Division of Hematology, Philadelphia, Pa. *Associate Professor of Medicine.* (4, 1940)

Miller, Frederick R., A.M., M.D., F.R.C.P. (C), F.R.S. Faculty of Medicine, University of Western Ontario, London, Ont., Canada. *Professor of Physiology.* (1, 1908)

Miller, G. H., A.M., M.D. American University of Beirut, Beirut, Syria. *Dean of the College of Medicine.* (3, 1925)

Miller, Lloyd C., Ph.D. Research and Biologic Laboratory, Winthrop Chemical Co., Rensselaer, N. Y. *Senior Pharmacologist.* (3, 1938)

Miller, R. C., Ph.D. Pennsylvania State College, State College. *Assistant Professor Agricultural and Biological Chemistry.* (5, 1935)

Miller, Zelma Baker, Ph.D. Department of Medicine, University of Chicago, Chicago, Ill. *Research Associate.* (2, 1940)

Millikan, Glenn A., Ph.D. Johnson Foundation, University of Pennsylvania, Philadelphia. *Fellow in Biophysics.* (1, 1940)

Mills, Clarence A., Ph.D., M.D. 5046 Oberlin Blvd., Cincinnati, O. *James T. Heady Professor of Experimental Medicine, University of Cincinnati.* (1, 1921; 2, 1921)

Minot, Annie Stone, Ph.D. Vanderbilt University Medical School, Nashville, Tenn. *Research Associate, Department of Pharmacology.* (1, 1923)

Mirsky, Alfred E., Ph.D. Hospital of the Rockefeller Institute, 66th St. and York Ave., New York City. *Associate Member, Rockefeller Institute.* (2, 1941)

Mirsky, I. Arthur, M.Sc., M.D., C.M. The Jewish Hospital, Cincinnati, O. *Director, The May Institute for Medical Research; Assistant Professor of Biochemistry, University of Cincinnati.* (1, 1936)

Mitchell, Harold H., M.S., Ph.D. Room 557, Old Agricultural Bldg., University of Illinois, Urbana. *Professor of Animal Nutrition.* (2, 1919; 5, 1933)

Mitchell, Helen S., Ph.D. 1321 S. Arlington Ridge Road, Arlington, Va. *Chief Nutritionist, Office of Foreign Relief and Rehabilitation.* (2, 1925; 5, 1933)

Mitchell, Philip H., Ph.D. Brown University, Providence 12, R. I. *Robert P. Brown Professor of Biology.* (2, 1909)

Molitor, Hans, M.D. 50 Lawrence St., Rahway, N. J. *Director, Merck Institute for Therapeut Research.* (1, 1933; 3, 1942)

Molomut, Norman, M.A., Ph.D. 200 Walnu St., Yellow Springs, O. *Assistant Bacterio ogist, Department of Medicine, Columbia Un versity (on leave); First Lieutenant, Army U. S. Aero Medical Research.* (6, 1942)

Moon, Virgil H., M.Sc., M.D. Jefferson Medic College, Philadelphia, Pa. *Professor of P thology.* (4, 1934)

Moore, A. R., Ph.D. University of Orego Eugene. *Research Professor of General Phys ology in the Department of Psychology.* (1, 191

Moore, Carl Vernon, M.D. Washington Unive sity School of Medicine, St. Louis, Mo. *Ass ciate Professor of Medicine.* (4, 1938; 5, 194

Moore, Lane A., Ph.D. University of Marylan College Park. *Research Assistant in Dai Husbandry.* (5, 1940)

Moore, Robert A., M.D. Washington Universit Medical School, St. Louis, Mo. *Professor Pathology.* (4, 1929)

Moore, Robert M., M.D. 5808 Westminster, S Lous, Mo. *Lt. Col., M.C.* (1, 1932)

Moorhouse, Victor Henry K., M.B. Universit of Manitoba, Winnipeg, Canada. *Professor Physiology.* (1, 1912)

Morgan, Agnes Fay, M.S., Ph.D. University California, Berkeley. *Professor of Home Ec nomics; Biochemist, Agric. Exp. Station; Hea Department of Home Economics.* (2, 1929; 1933)

Morgan, Clifford T., M.A., Ph.D.* Harvard Uni versity, Cambridge, Mass. *Faculty Instructor i Physiological Psychology.* (1, 1943)

Morgulis, Sergius, A.M., Ph.D. University o Nebraska College of Medicine, Omaha. *Pro fessor of Biochemistry.* (1, 1914; 2, 1916)

Morison, Robert S., M.D. Harvard Medica School, Boston, Mass. *Assistant Professor o Anatomy.* (1, 1938)

Moritz, Alan R., M.D. Harvard Medical School Boston, Mass. *Professor of Legal Medicine* (4, 1934)

Morrell, Clarence Allison, M.A., Ph.D. Department of Pensions and National Health, Laboratory of Hygiene, Sussex and John Sts., Ottawa, Canada. *Senior Pharmacologist.* (3, 1937)

Morris, Harold P. National Cancer Institute, National Institute of Health, Bethesda, Md. (5, 1943)

Morris, Marion C., M.S., Ph.D. Department of Plant Science, Vassar College, Poughkeepsie, N. Y. (6, 1936)

Morrison, Dempsie B., M.S., Ph.D. University of Tennessee College of Medicine, Memphis. *Associate Professor of Chemistry.* (2, 1936)

Morse, Minerva, M.S., Ph.D. 5525 Kimbark Ave., Chicago, Ill. *Research Associate, Department of Pediatrics, University of Chicago.* (2, 1934)

Morse, Withrow, Ph.D. 32 Manchester Rd., Eastchester, via Tuckahoe, N. Y. *Consultant.* (2, 1914)

Mortimer, Bernard, Ph.D., M.D. Cook County Hospital, Chicago, Ill. (1, 1936)

Morton, John J., M.D. University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. *Professor of Surgery.* (4, 1927)

Mosenthal, Herman O., M.D. 889 Lexington Ave., New York City. *Professor of Medicine, New York Post-Graduate Medical School.* (2, 1915)

Moulton, C. Robert, Ph.D. 5717 Kenwood Ave., Chicago, Ill. *Editor.* (5, 1933)

Moyer, Carl A., Ph.D.* University of Michigan, Medical School, Ann Arbor. *Assistant Professor of Surgery.* (1, 1913)

Mudd, Stuart, M.A., M.D. University of Pennsylvania, Philadelphia. *Professor of Bacteriology.* (1, 1921; 4, 1927; 6, 1927)

Muehlberger, Clarence W., M.S., Ph.D. State Health Department Laboratories, Lansing, Mich. *State Toxicologist.* (3, 1928)

Mueller, J. Howard, M.S., Ph.D. 2176 Centre St., W. Roxbury, Mass. *Professor of Bacteriology and Immunology, Harvard Medical School.* (2, 1922; 4, 1927; 6, 1920)

Mukherji, B., M.B., D.Sc. All-India Institute of Hygiene and Public Health, Calcutta. *Director, Biochemical Standardization Laboratory.* (3, 1938)

Mulder, Arthur G., Ph.D. University of Tennessee College of Medicine, Memphis. *Associate Professor of Physiology.* (1, 1937)

Mulinos, M. G., M.D., Ph.D. College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City. *Associate Professor of Pharmacology.* (3, 1931)

Mull, James W., Ph.D. Maternity Hospital, 2065 Adelbert Rd., Cleveland, O. *Senior Instructor in Biochemistry in charge of Biochemical Research in Obstetrics, Western Reserve University.* (2, 1937)

Mullin, F. J., M.S., Ph.D. University of Chicago, Chicago, Ill. *Assistant Professor of Physiology.* (1, 1937)

Munsell, Hazel E., M.A., Ph.D. Havemeyer Hall, Columbia University, New York City. (5, 1933)

Muntwyler, Edward, Ph.D. Western Reserve University, 2109 Adelbert Rd., Cleveland, O. *Professor of Experimental Biochemistry.* (2, 1931)

Murlin, John R., A.M., Ph.D., Sc.D. University of Rochester Medical School, 260 Crittenden Blvd., Rochester, N. Y. *Lewis P. Ross Professor of Physiology and Director of Department of Vital Economics.* (1, 1906; 2, 1908; 5, 1933)

Murphy, James B., M.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member.* (4, prior to 1920)

Murray, Everitt G. D., O.B.E., B.A. honors in Natural Science, M.A., L.M.S.S.A., F.R.S.C. McGill University, Montreal, Canada. *Professor of Bacteriology and Immunology and Head of the Department, McGill University; Bacteriologist-in-Chief to the Royal Victoria Hospital, to the Children's Memorial Hospital and to the Alexandra Hospital.* (6, 1933)

Myers, Chester N., Ph.D., Sc.D. 34 Cedar Place, Yonkers 5, N. Y. *Chief, Division Chemotherapy, N. Y. Skin and Cancer Hospital; Associate in Dermatology and Syphilology, College of Physicians and Surgeons; Research Chemist, Vanderbilt Clinic; Director, Chemical and Clinical Research, H. A. Metz Laboratories, Inc.* (2, 1922)

Myers, Victor C., M.A., Ph.D., Sc.D. School of Medicine, Western Reserve University, Cleveland, O. *Professor and Director of Biochemistry.* (1, 1916; 2, 1910; 5, 1933)

Nachmansohn, David, M.D. Laboratory of Physiology, School of Medicine, Yale University, New Haven, Conn. (1, 1940)

Nadler, J. Ernest, M.D., Med.D.Sc. 477 First Ave., New York City. *Instructor in Medicine.* (3, 1940)

Nahum, Louis N., M.D. 1142 Chapel St., New Haven, Conn. *Assistant Professor of Physiology, Yale University.* (1, 1934)

Nash, Thomas P., Jr., M.A., Ph.D. 875 Monroe Ave., Memphis, Tenn. *Professor of Chemistry, College of Medicine; Dean of School of Biological Sciences, University of Tennessee.* (2, 1923)

Nasset, Edmund S., M.S., Ph.D. University of Rochester, 260 Crittenden Blvd., Rochester, N. Y. *Associate Professor of Physiology; Major, San. Corps.* (1, 1932; 5, 1940)

Nathanson, Ira T., M.S., M.D.* Massachusetts General Hospital, Boston. *Instructor in Surgery, Harvard Medical School; Assistant in Surgery, Mass. General Hospital.* (1, 1943)

Nathanson, Morris D., M.D. 658 S. Bonnie Brae St., Los Angeles, Calif. *Associate Clinical Professor of Medicine, University of Southern California School of Medicine.* (3, 1940)

Necheles, Heinrich, M.D., Ph.D. Michael Reese Hospital, Chicago, Ill. *Director, Dept. of Gastro-intestinal Physiology, Michael Reese Hospital; Professorial Lecturer in Physiology, University of Chicago.* (1, 1929)

Neill, James M., Ph.D. Medical College, Cornell University, 1300 York Ave., New York City.

Professor of Bacteriology and Immunology. (6, 1930)

Neilson, Charles Hugh, A.M., Ph.D., M.D. Humboldt Building, St. Louis, Mo. *Associate Dean and Professor of Medicine, St. Louis University Medical School.* (2, 1906)

Nelson, Arthur A., M.D., Ph.D. Food and Drug Administration, Federal Security Agency, Washington, D. C. *Senior Pathologist, Division of Pharmacology.* (4, 1942)

Nelson, Carl Ferdinand, M.D., Ph.D. Department of Biochemistry, University of Kansas, Lawrence. *Professor of Physiological Chemistry.* (2, 1914)

Nelson, Erwin E., Ph.D., M.D. The Burroughs Wellcome and Co., Experimental Research Laboratories, Tuckahoe, N. Y. *Director of Research Laboratories.* (1, 1923; 3, 1924)

Nelson, E. M., M.S., Ph.D. Food and Drug Administration, Federal Security Agency, Washington 25, D. C. *Chief, Vitamin Division.* (2, 1927; 5, 1933)

Nelson, John B., Ph.D. Rockefeller Institute for Medical Research, Princeton, N. J. *Associate Member.* (4, 1934)

Nelson, John M., Ph.D. Columbia University, New York City. *Professor of Organic Chemistry.* (2, 1923)

Nelson, P. Mabel, M.S., Ph.D. Iowa State College, Ames. *Professor and Head of Department of Foods and Nutrition.* (5, 1934)

Nelson, Tell, M.A., M.D. 1st Station Hospital, A.P.O. 915, % Postmaster, San Francisco, Calif. *Major, M. C., U. S. A.* (6, 1938)

Nelson, Victor E., M.S. Iowa State College, Ames. *Professor of Physiological Chemistry.* (2, 1924; 5, 1933);

Nelson, Warren O., M.S., Ph.D. Wayne University College of Medicine, Detroit, Mich. *Professor of Anatomy.* (1, 1937)

Neter, Erwin, M.D. School of Medicine, University of Buffalo, 24 High St., Buffalo, N. Y. *Attending Bacteriologist, Children's Hospital.* (6, 1937)

Nettleship, Anderson, M.D. National Cancer Institute, National Institute of Health, U. S. Public Health Service, Bethesda, Md. *Passed Assistant Surgeon.* (R) (4, 1942)

Neurath, Hans, Ph.D. School of Medicine, Duke University, Durham, N. C. *Assistant Professor of Biochemistry.* (2, 1940)

Neuwelt, Frank, M.D. 504 Broadway, Gary, Ind. *Research Associate, Department of Gastrointestinal Research, Michael Reese Hospital.* (1, 1940)

Neuwirth, Isaac, Ph.D. 209 E. 23rd St., New York City. *Associate Professor of Pharmacology and Therapeutics, New York University College of Dentistry.* (2, 1924; 3, 1931)

Newburgh, L. H., M.D. University of Michigan, Ann Arbor. *Professor Clinical Investigation, Medical School.* (5, 1933)

Nice, Leonard B., Ph.D. Chicago Medical School, 710 S. Wolcott Ave., Chicago, Ill. *Professor of Physiology and Pharmacology.* (1, 1921)

Nicholas, John S., M.S., Ph.D. Osborn Zoological Laboratory, Yale University, New Haven, Conn. *Bronson Professor of Comparative Anatomy.* (1, 1927)

Nicholson, Hayden C., M.S., M.D. University of Michigan, Ann Arbor. *Associate Professor of Physiology. Captain, 29th Altitude Training Unit, San Antonio Aviation Cadet Center, San Antonio, Texas.* (1, 1932)

Nicolet, Ben H., Ph.D. Bureau of Dairy Industry, U. S. Department of Agriculture, Beltsville, Md. *Senior Chemist.* (2, 1932)

Niemann, Carl G., Ph.D. California Institute of Technology, Pasadena 4, Calif. *Associate Professor, Organic Chemistry.* (2, 1940)

Nigg, Clara, M.A., Ph.D. Camp Detrick, Frederick, Md. (6, 1929)

Nims, Leslie F., M.A., Ph.D. Yale University School of Medicine, 333 Cedar St., New Haven, Conn. *Assistant Professor of Physiology.* (1, 1940)

Noble, Robert Laing, M.D., Ph.D. Research Institute of Endocrinology, McGill University, Montreal, Canada. *Research Assistant.* (1, 1941)

Nord, F. F., Ph.D. Fordham University, New York City. *Professor of Chemistry.* (2, 1940)

Norris, Earl R., Ph.D. University of Washington, Seattle. *Professor of Chemistry.* (2, 1938)

Norris, L. C., Ph.D. Rice Hall, Cornell University, Ithaca, N. Y. *Professor of Nutrition; Secretary, School of Nutrition.* (2, 1939; 5, 1934)

Northrop, J. H., M.A., Ph.D., Sc.D., LL.D. Rockefeller Institute for Medical Research, Princeton, N. J. *Member.* (2, 1938)

Northup, David W., M.A., Ph.D. West Virginia University Medical School, Morgantown. *Associate Professor of Physiology.* (1, 1936)

Novy, F. G., M.D., Sc.D., LL.D. 721 Forest Ave., Ann Arbor, Mich. *Dean Emeritus of the Medical School and Professor Emeritus of Bacteriology, University of Michigan; Member, National Academy of Sciences.* (2, 1906)

Nye, Robert N., M.D. 32 Lawrence Rd., Chestnut Hill, Mass. *Editor, New England Journal of Medicine.* (6, 1923)

Oberst, Fred W., M.S., Ph.D. U. S. Public Health Service Hospital, Lexington, Ky. *Biological Chemist.* (2, 1936)

Ochoa, Severo, M.D. New York University College of Medicine, New York City. *Research Associate in Medicine.* (2, 1942)

Ogden, Eric, M.R.C.S. (England), L.R.C.P. (London). University of California, Berkeley. *Assistant Professor of Physiology.* (1, 1911)

O'Hare, James P., M.D. 520 Commonwealth Ave., Boston, Mass. *Physician, Peter Bent Brigham Hospital; Assistant Professor of Medicine, Harvard Medical School.* (4, 1927)

Okey, Ruth, Ph.D. 1583 Life Sciences Bldg., University of California, Berkeley. *Associate Professor of Home Economics; Associate Biochemist, State Exp. Station, College of Agriculture* (2, 1922; 5, 1933)

Olcott, Harold S., M.S., Ph.D. Western Regional Research Laboratory, U. S. Department of Agriculture, Albany 6, Calif. *Senior Chemist.* (2, 1935)

Oldham, Frances Kathleen, M.S., Ph.D. University of Chicago, Chicago, Ill. *Research Assistant in Pharmacology.* (3, 1941)

Olitsky, Peter K., M.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member.* (4, 1923; 6, 1917)

Oliver, Jean Redman, M.D. Hoagland Laboratory, 335 Henry St., Brooklyn, N. Y. *Professor of Pathology, Long Island College of Medicine.* (1, 1924; 4, 1924)

Oliver, Wade W., M.D. Hoagland Laboratory, 335 Henry St., Brooklyn, N. Y. *Professor of Bacteriology, Long Island College of Medicine.* (4, 1925)

Olmsted, J. M. D., M.A., Ph.D. University of California, Berkeley. *Professor of Physiology.* (1, 1920)

Olson, Carl, Jr., D.V.M., Ph.D. Massachusetts State College, Amherst. *Research Professor of Veterinary Science.* (4, 1937)

Opie, Eugene L., M.D., Sc.D., LL.D. Cornell University Medical College, 1300 York Ave., New York City. *Member, National Academy of Sciences.* (1, 1906; 4, prior to 1920; 6, 1923)

Oppenheimer, Enid Tribe. 124 E. 61st St., New York City. *Instructor in Physiology, Columbia University.* (1, 1932)

Oppenheimer, Morton Joseph, Ed.M., M.D. 3400 N. Broad St., Philadelphia, Pa. *Associate Professor of Physiology, Temple University School of Medicine.* (1, 1942)

Orent-Keiles, Elsa, D.Sc. Bureau of Human Nutrition and Home Economics, U. S. Department of Agriculture, Beltsville, Md. *In Charge of Nutrition Investigations; Assistant Chief, Foods and Nutrition Division.* (2, 1935; 5, 1935)

Ort, John M., Ph.D. 356 Raymond St., Rockville Centre, Long Island, N. Y. *Research Chemist, E. R. Squibb and Sons Co.* (2, 1932)

Orten, James M., M.S., Ph.D. Wayne University College of Medicine, Detroit, Mich. *Assistant Professor of Physiological Chemistry.* (2, 1936; 5, 1937)

Orth, O. Sidney, M.S., Ph.D., M.D. University of Wisconsin Medical School, Madison. *Assistant Professor of Pharmacology.* (1, 1942)

Osborne, Stafford L., B.P.E., M.S., Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Assistant Professor of Physical Therapy.* (1, 1941)

Oster, Robert H., Ph.D. University of Maryland Medical School, Greene and Lombard Sts., Baltimore. *Assistant Professor of Physiology.* (1, 1938)

Osterberg, Arnold E., M.S., Ph.D. Mayo Clinic, Rochester, Minn. *Head, Clinical Biochemistry; Associate Professor, Mayo Foundation.* (2, 1933)

Osterhout, W. J. V., Ph.D. Rockefeller Institute, 66th St. and York Ave., New York City. *Member Emeritus of the Institute; Member of the National Academy of Sciences.* (1, 1910)

Owen, Seward E., M.S., Ph.D. 418 So. 20th Ave., Maywood, Ill. *Major, S. E. San. Corps.* (1, 1938)

Pack, George T., M.D. 155 East 72nd St., New York City. *Fellow in Cancer Research, Memorial Hospital.* (1, 1924)

Page, Irvine H., M.D. Indianapolis City Hospital, Indianapolis, Ind. *Director of Clinical Research.* (1, 1937; 2, 1932)

Painter, Elizabeth E., Ph.D. College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City. *Instructor in Physiology.* (1, 1941)

Palmer, Albert H., Ph.D. Pennsylvania State College School of Agriculture, State College. *Assistant Professor of Biochemistry.* (2, 1934)

Palmer, Leroy S., A.M., Ph.D. Snyder Hall, University Farm, St. Paul, Minn. *Professor and Chief of the Division of Agricultural Biochemistry, University of Minnesota.* (2, 1920; 5, 1933)

P'An, S. Y., M.D. Peiping Union Medical College, Peiping, China. *Assistant in Pharmacology.* (3, 1941)

Pangborn, Mary C., Ph.D. 20 Morris St., Albany, N. Y. *Assistant Biochemist, New York State Department of Health, Division of Laboratories and Research.* (2, 1941)

Pappenheimer, Alwin M., M.D. 630 W. 168th St., New York City. *Professor of Pathology, Columbia University.* (4, 1922)

Pappenheimer, Alwin, M., Jr., Ph.D. Harvard Medical School, Boston, Mass. *Captain, Sanitary Corps, A.U.S.* (2, 1941; 6, 1938)

Park, Edwards A., M.D. Johns Hopkins Hospital, Baltimore, Md. *Professor of Pediatrics, Johns Hopkins University.* (4, 1923)

Parker, George Howard, Sc.D. 16 Berkeley St., Cambridge, Mass. *Professor of Zoology Emeri-*

tus, Harvard University; Member of the National Academy of Sciences. (1, 1900)

Parker, Robert F., M.D. Lakeside Hospital, 2065 Adelbert Rd., Cleveland, O. *Associate Professor of Medicine.* (4, 1942; 6, 1935)

Parkins, William M., M.A., Ph.D. School of Medicine, University of Pennsylvania, Philadelphia. *Research Fellow, Harrison Department of Surgical Research.* (1, 1939)

Parpart, Arthur K., Ph.D. Guyot Hall, Princeton University, Princeton, N. J. *Associate Professor of Physiology.* (1, 1937)

Parr, Leland W., Ph.D. The George Washington University School of Medicine, 1335 H St., N.W. Washington, D. C. *Professor of Bacteriology.* (4, 1940)

Parsons, Helen T., M.S., Ph.D. University of Wisconsin, Madison. *Professor of Home Economics; In Charge of Purnell Research in Nutrition.* (2, 1929; 5, 1933)

Parsons, Robert J., M.D. University of Michigan, Ann Arbor. *Assistant Professor of Pathology.* (4, 1939)

Paschkis, Karl E., M.D. 1025 Walnut St., Philadelphia, Pa. *J. Ewing Mears Fellow in Physiology and Medicine, Jefferson Medical College; Chief Clinical Assistant, Endocrine Clinic, Jefferson Medical College Hospital.* (1, 1942)

Patterson, Thos. L., A.M., M.S., Ph.D. Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich. *Professor of Physiology.* (1, 1920)

Paul, John R., M.D., A.M. 330 Cedar St., New Haven, Conn. *Professor of Preventive Medicine, Yale University Medical School.* (4, 1927; 6, 1937)

Pearce, John Musser, M.D. Long Island College of Medicine, Hoagland Laboratory, 335 Henry St., Brooklyn, N. Y. *Associate Professor of Pathology.* (4, 1942)

Pearce, Louise, M.D. Rockefeller Institute for Medical Research, Princeton, N. J. *Associate Member in Pathology and Bacteriology.* (3, 1915; 4, 1925)

Pearcy, Frank, Ph.D., M.D. 471 Park Ave., New York City. (1, 1928)

Pearse, Herman E., M.D. School of Medicine and Dentistry, University of Rochester, Crittenden Blvd., Rochester, N. Y. *Associate Professor of Surgery.* (4, 1932)

Pearson, Paul B., Ph.D. Texas A. & M. College, College Station. *Professor in charge of Animal Nutrition.* (5, 1940)

Pease, Marshall C., Jr., M.D. 155 E. 62nd St., New York City. *Clinical Professor of Pediatrics, New York Post-Graduate Medical School and Hospital, Columbia University.* (6, 1920)

Pemberton, Ralph, M.S., M.D. University of Pennsylvania, Philadelphia. *Professor of Medicine, Graduate School of Medicine.* (5, 1933)

Penfield, Wilder G., M.D., D.Sc. McGill University, Montreal, Que., Canada. *Professor of Neurology and Neurosurgery.* (1, 1932)

Pennington, Mary Engle, Ph.D. 233 Broadway, New York 7, N. Y. *Consultant in Connection with the Handling, Transportation and Storage of Perishables.* (2, 1908)

Peoples, S. Anderson, M.D. Baylor University College of Medicine, Houston, Texas. *Professor of Pharmacology.* (3, 1937)

Perlzweig, William A., A.M., Ph.D. Box 3711, Duke Hospital, Durham, N. C. *Professor of Biochemistry, Duke University; Biochemist, Duke Hospital.* (2, 1924)

Permar, Howard H., M.D. Pathologic Laboratories, Mercy Hospital, Pittsburgh, Pa. *Director of Laboratories.* (4, 1925)

Peters, John P., M.D. 123 Marvel Road, New Haven 15, Conn. *Sterling Professor of Medicine, Yale University.* (2, 1922)

Petersen, William F., M.D. 1322 Astor St., Chicago, Ill. *Professor of Pathology, University of Illinois.* (3, 1923; 4, 1923)

Peterson, William H., A.M., Ph.D. Biochemistry Building, University of Wisconsin, Madison. *Professor of Biochemistry.* (2, 1919; 5, 1936)

Petroff, S. A., Ph.D., Sc.D. Sea View Hospital, West New Brighton, Staten Island, N. Y. *Director of Bacteriology and Immunology.* (6, 1926)

Pett, L. B., M.D., Ph.D. Nutrition Services, Department of Pensions and National Health, Ottawa, Canada. *Director.* (2, 1937)

Peugnet, Hubert B., M.D. 4530 McPherson, St. Louis, Mo. *Major, M.C.* (1, 1938)

Pfeiffer, Carl C., Ph.D., M.D. Naval Medical Research Institute, Bethesda, Md. *Lieutenant, M.C., U.S.N.R.* (3, 1938)

Pfiffner, Joseph J., Ph.D. 1007 Lincoln Ave., Ann Arbor, Mich. *Research Chemist, Parke, Davis & Co., Detroit.* (1, 1931; 2, 1931)

Phatak, Nilkanth M., M.S., Ph.D. North Pacific College of Oregon, School of Dentistry, Portland. *Associate Professor of Physiology, Pharmacology, and Research; and Instructor, Dept. of Pharmacology, University of Oregon Medical School, Portland.* (3, 1941)

Phillips, Paul H., Ph.D. University of Wisconsin, Madison. *Professor of Biochemistry.* (2, 1940; 5, 1938)

Phillips, Robert Allan, M.D. Rockefeller Institute for Medical Research, New York City. *Fellow.* (1, 1938)

Pick, Ernst Peter, M.D. 19 E. 98th St., New York City. *Associate Pharmacologist to the Mt.*

Sinai Hospital; Clinical Professor of Pharmacology in Columbia University. (3, 1940)

Pierce, Harold B., M.S., Ph.D. College of Medicine, University of Vermont, Burlington. *Professor and Head of Physiological Chemistry.* (2, 1929; 5, 1933)

Pierce, Harold Fisher, Ph.D., M.D. Station Hospital, Randolph Field, Texas. *Major, S.C.* (1, 1928)

Pierce, Ira H., M.S., Ph.D. Univ. of Iowa, Iowa City. *Associate Professor of Pharmacology.* (3, 1933)

Pike, Frank H., Ph.D. 630 W. 168th St., New York City. *Associate Professor of Physiology, Columbia University.* (1, 1907)

Pilcher, J. Douglas, M.D. City Hospital, Scranton Road, Cleveland, O. *Associate Professor of Pediatrics, Western Reserve Medical School.* (1, 1912; 3, 1911)

Pillemer, Louis, Ph.D. Box 195, Room 111, Army Medical School, Army Medical Center, Washington, D. C. *First Lieutenant, Sanitary Corps, U. S. A.* (6, 1942)

Pincus, Gregory, M.S., Sc.D. Clark University, Worcester, Mass. *Visiting Professor of Experimental Zoology.* (1, 1935)

Pinkerton, Henry, M.D. St. Louis University School of Medicine, St. Louis, Mo. *Professor of Pathology.* (4, 1931)

Pinkston, James O., Ph.D. c/o Mrs. James O. Pinkston, Near East College Assn., 50 W. 50th St., New York, N. Y. (1, 1936; 3, 1939)

Pinson, Ernest A., Ph.D.* Biophysics Branch, Aeromedical Laboratory, Wright Field, Dayton, O. *1st. Lt. Air Corps.* (1, 1943)

Pittman, Martha S., A.M., Ph.D. Kansas State College, Manhattan. *Head of Department of Food Economics and Nutrition.* (5, 1933)

Pitts, Robert F., Ph.D., M.D. New York University College of Medicine, 477 First Ave., New York City. *Assistant Professor of Physiology.* (1, 1934)

Plass, Everett D., M.D. University Hospital, Iowa City, Iowa. *Professor and Head of Department of Obstetrics and Gynecology, State University of Iowa.* (2, 1922)

Plotz, Harry, M.D. Army Medical School, Army Medical Center, Washington, D. C. *Chief of Virus and Rickettsial Laboratory.* (6, 1917)

Pohlman, Augustus G., M.D. 2202 W. Third St., Los Angeles, Calif. *Associate Clinical Professor, Department of Otolaryngology, University of Southern California School of Medicine.* (1, 1934)

Pollack, Herbert, Ph.D., M.D. 20 E. 76th St., New York City. *Associate in Medicine and Physician in Charge of Metabolism Clinics, Mt. Sinai Hospital.* (1, 1933; 5, 1935)

Pond, Samuel E., A.M., Ph.D. U. S. Naval Research Laboratory, Anacostia Station, Washington, D. C. 1203 Enfield St., R. F. D., Thompsonville, Conn. (1, 1924)

Ponder, Eric, M.D., Sc.D. The Nassau Hospital, Mineola, Long Island, N. Y. (1, 1931)

Popper, Hans, M.S., M.D. University of Illinois College of Medicine, 1825 W. Harrison St., Chicago. *Director of the Hektoen Institute for Medical Research of Cook County Hospital.* (4, 1942)

Porter, Eugene L., A.M., Ph.D. University of Texas, Medical Branch, Galveston. *Professor of Physiology.* (1, 1913)

Porter, William Townsend, M.D., Sc.D., LL.D. Dover, Mass. *Professor Emeritus of Comparative Physiology, Harvard University.* (1, 1891)

Potter, Truman S., M.D. University of Chicago, Chicago, Ill. *Research Associate in Preventive Medicine.* (6, 1939)

Potter, Van Rensselaer, M.S., Ph.D. McArdle Memorial Laboratory, University of Wisconsin Medical School, Madison. *Assistant Professor of Oncology.* (2, 1941)

Povitzky, Olga R., M.D., D.P.H. 235 E. 22nd St., New York City. *Bacteriologist, Bureau of Laboratories, New York City Department of Health.* (6, 1920)

Powell, Horace M., Sc.D. 5565 Washington Blvd., Indianapolis, Ind. *Bacteriologist, Eli Lilly & Co.* (6, 1934)

Power, Marschelle H., M.S., Ph.D. Mayo Clinic, Rochester, Minn. *Associate Professor of Physiological Chemistry, Mayo Foundation, University of Minnesota.* (2, 1932)

Del Pozo, E. C., M.D.* Harvard Medical School, Boston, Mass. *Research Fellow, Harvard Medical School.* (1, 1943)

Pratt, Frederick H., A.M., M.D. 80 E. Concord St., Boston, Mass. *Professor of Physiology, Boston University School of Medicine.* (1, 1919)

Pratt, Joseph H., A.M., M.D. New England Medical Center, 25 Bennet St., Boston, Mass. *Physician-in-Chief, Boston Dispensary, and Joseph H. Pratt Diagnostic Clinic; Professor of Clinical Medicine, Tufts Medical School.* (1, 1910; 3, 1910; 4, 1927)

Preisler, Paul W., M.S., Ph.D. 3420 Longfellow Blvd., St. Louis, Mo. *Major, Sn.C., Brooke General Hospital, Fort Sam Houston, Texas.* (2, 1931)

Prinzmetal, Myron, M.A., M.D. 2007 Wilshire Blvd., Los Angeles, Calif. *Instructor in Medicine and Lecturer in Physiology, University of Southern California Medical School.* (3, 1941)

Prosser, C. Ladd, Ph.D. University of Illinois, Urbana. *Assistant Professor of Zoology.* (1, 1935)

Pucher, George W., Ph.D. Connecticut Agricultural Experiment Station, New Haven. *Research Associate.* (2, 1927)

Puestow, Charles B., M.D., M.S., Ph.D. University of Illinois, College of Medicine, 1853 W. Polk St., Chicago. *Assistant Professor of Surgery.* (1, 1934)

Pugsley, Leonard I., Ph.D. Department of Pensions and National Health, Laboratory of Hygiene, Ottawa, Canada. *Pharmacologist.* (2, 1937)

Queen, Frank B., M.D. Passavant Memorial Hospital, Chicago, Ill. *Assistant Professor of Pathology, Northwestern University Medical School; Assistant Director, Patterson Cancer Clinic of Northwestern University Medical School, and Director, Patterson Laboratory for Cancer, Research, Passavant Memorial Hospital; Director of Laboratories, Passavant Memorial Hospital.* (4, 1941)

Quick, Armand J., M.D., Ph.D. 561 N. 15th St., Milwaukee, Wis. *Associate Professor of Pharmacology, Marquette Medical School.* (2, 1932; 3, 1937)

Quigley, J. P., Ph.D. Western Reserve University, Cleveland, O. *Professor of Gastro-Intestinal Physiology.* (1, 1929)

Quinby, William Carter, M.D. Peter Bent Brigham Hospital, Boston, Mass. *Clinical Professor of Genito-urinary Surgery, Harvard Medical School.* (1, 1916)

Quinn, Edmond John, Ph.D. 106 N. Lee Ave., Rockville Center, Long Island, N. Y. *Medicinal Sales Division, Merck & Co., Inc., Rahway, N. J.* (2, 1927; 5, 1933)

Rabinowitch, I. M., D.Sc., M.D., C.M., F.R.C.P., F.A.C.P. The Montreal General Hospital, Montreal, Canada. *Associate Professor of Medicine and Lecturer in Biochemistry, McGill University; Director, Department of Metabolism, Montreal General Hospital.* (2, 1928; 5, 1933)

Rackemann, Francis M., M.D. 263 Beacon St., Boston, Mass. *Physician, Massachusetts General Hospital; Lecturer in Medicine, Harvard Medical School.* (6, 1923)

Raffel, Sidney, Sc.D., M.D. Department of Bacteriology and Experimental Pathology, Stanford University, Calif. *Assistant Professor.* (6, 1938)

Raiziss, George W., Ph.D. 1720 Lombard St., Philadelphia, Pa. *Professor of Chemotherapy, Graduate School of Medicine, and Director, Dermatological Research Laboratory, University of Pennsylvania.* (2, 1913)

Rake, Geoffrey W., M.B., M.R.C.S., L.R.C.P. Division of Microbiology, The Squibb Institute for Medical Research, New Brunswick, N. J. *Head, Division of Microbiology.* (6, 1939)

Rakestraw, Norris W., A.M., Ph.D. Brown University, Providence, R. I. *Associate Professor of Chemistry.* (2, 1925)

Rakieten, Nathan, Ph.D. 4 Hillhouse Ave., New Haven, Conn. *Instructor in Applied Physiology, Yale University.* (1, 1941)

Ralli, Elaine P., M.D. 477 First Ave., New York City. *Associate Professor of Medicine, New York University College of Medicine.* (1, 1934; 5, 1933)

Ramsey, Robert Weberg, M.S., Ph.D. School of Medicine and Dentistry, University of Rochester, Rochester, N. Y. *Associate in Physiology.* (1, 1939)

Randall, Lowell O., Ph.D. Burroughs Wellcome Co., Tuckahoe, N. Y. *Pharmacologist.* (2, 1939)

Randall, Walter C., M.S., Ph.D.* St. Louis University, School of Medicine, 1402 S. Grand Blvd., St. Louis, Mo. *Instructor in Physiology.* (1, 1943)

Rane, Leo, Ph.D. Lederle Laboratories, Inc., Pearl River, N. Y. *Department Head, Normal Blood Plasma.* (6, 1942)

Rapoport, Samuel, M.D., Ph.D. The Children's Hospital Research Foundation, Elland and Bethesda, Cincinnati, O. *Research Associate.* (2, 1941)

Rapport, David, M.D. 416 Huntington Ave., Boston, Mass. *Professor of Physiology, Tufts College Medical School.* (1, 1922)

Rasmussen, Andrew Theodore, Ph.D. University of Minnesota Medical School, Minneapolis. *Professor of Neurology.* (1, 1919)

Ratner, Bret, M.D. New York University College of Medicine, 50 E. 78th St., New York City. *Professor of Pediatrics.* (4, 1940; 6, 1928)

Raulston, B. O., M.D. 200 S. Hudson Ave., Los Angeles, Calif. *Professor of Medicine, Director of Clinical Teaching, and Associate Dean, the University of Southern California, School of Medicine.* (3, 1942)

Ravdin, I. S., M.D. University of Pennsylvania School of Medicine, Philadelphia. *Harrison Professor of Surgery; Surgeon, Hospital of the University of Pennsylvania.* (1, 1930; 4, 1930)

Ray, George B., A.M., Ph.D. Long Island College of Medicine, 350 Henry St., Brooklyn, N. Y. *Professor of Physiology and Pharmacology.* (1, 1924)

Raymond, Albert L., Ph.D. G. D. Searle & Co., P. O. Box 5110, Chicago 80, Ill. *Director of Research.* (2, 1932)

Redfield, Alfred C., Ph.D. Woods Hole, Mass. *Professor of Physiology, Harvard University.* (1, 1919)

Reed, Carlos Isaac, A.M., Ph.D. College of Medicine, University of Illinois, 1853 W. Polk St., Chicago. *Professor of Physiology.* (1, 1923)

Reed, Howard S., Ph.D. 3018 Life Sciences Bldg., University of California, Berkeley. *Professor of Plant Physiology.* (2, 1909)

Rees, Maurice Holmes, A.M., Ph.D., M.D. University of Colorado School of Medicine, Denver. *Professor of Physiology and Pharmacology; Dean of the University of Colorado School of Medicine and Hospitals.* (1, 1922)

Reid, Marion Adelaide, A.M., Ph.D. 80 E. Concord St., Boston, Mass. *Instructor in Physiology, Boston University.* (1, 1941)

Reimann, Hobart A., M.D. Jefferson Hospital, Philadelphia, Pa. *Professor of Medicine, Jefferson Medical College.* (4, 1933)

Reimann, Stanley P., M.D., Sc.D. 703 W. Phil-Ellena St., Mount Airy, Philadelphia, Pa. *Director of the Research Institute of the Lankenau Hospital; Associate Professor of Surgical Pathology, Graduate School of Medicine, University of Pennsylvania; Professor of Oncology, Hahnemann Medical College and Hospital, Philadelphia.* (1, 1921; 4, 1924)

Reiner, Laszlo, M.D., Ph.D. Research Division, Wallace & Tiernan Co., Inc., Belleville, N. J. (2, 1942; 6, 1933)

Reinhold, John G., M.S., Ph.D. Philadelphia General Hospital, 34th St. and Curie Ave., Philadelphia, Pa. *Chief Biochemist; Instructor in Physiological Chemistry, University of Pennsylvania.* (2, 1936)

Remington, John W., M.S., Ph.D.* University of Georgia, School of Medicine, Augusta. *Assistant Professor of Physiology.* (1, 1943)

Remington, Roe E., M.A., Ph.D., D.Sc. Medical College of South Carolina, Charleston. *Professor of Nutrition and Director of Food Research Laboratory.* (2, 1930; 5, 1934)

Renfrew, Alice G., Ph.D. Mellon Institute of Industrial Research, University of Pittsburgh, Pittsburgh, Pa. *Fellow, Department of Research in Pure Chemistry.* (2, 1939)

Renshaw, Birdsey, M.A., Ph.D. Oberlin College, Oberlin, O. *Assistant Professor of Physiology.* (1, 1941)

Reynolds, Chapman, M.D. Louisiana State University, New Orleans. *Assistant Professor of Pharmacology.* (3, 1937)

Reynolds, Samuel R. M., Ph.D. Department of Embryology, Carnegie Institution of Washington, Wolfe and Madison Sts., Baltimore, Md. *Research Associate.* (1, 1932)

Reznikoff, Paul, M.D. New York Hospital, 525 E. 68th St., New York City. *Associate Professor of Clinical Medicine, Cornell University Medical College.* (1, 1927)

Rhoads, Cornelius Packard, M.D. Memorial Hospital, 444 E. 68th St., New York City. *Director.* (4, 1930)

Rice, Christine E., M.A., Ph.D. Department of Bacteriology, Queen's University, Kingston, Ontario, Canada. (6, 1938)

Rice, James C., A.M., Ph.D. University of Mississippi, P. O. Box 475, University. *Professor of Pharmacology.* (3, 1941)

Rich, Arnold Rice, M.D. Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Pathology, Johns Hopkins University.* (4, 1924)

Richards, Alfred N., A.M., Ph.D., Sc.D., M.D. (hon.), LL.D. University of Pennsylvania Medical School, Philadelphia. *Professor of Pharmacology and Vice-President in Charge of Medical Affairs; Member, National Academy of Sciences.* (1, 1900; 2, 1906; 3, 1909)

Richards, Oscar W., M.A., Ph.D. Research Department, Spencer Lens Co., 19 Doat St., Buffalo, N. Y. *Research Biologist.* (1, 1934)

Richards, Richard Kohn, M.D. Abbott Laboratories, North Chicago, Ill. *Chief Pharmacologist.* (1, 1938)

Richardson, Arthur P., M.D. University of Tennessee Medical School, Memphis. *Associate Professor and Head, Department of Pharmacology.* (3, 1939)

Richardson, Luther R., Ph.D. University of Missouri, Columbia. *Instructor in Agricultural Chemistry.* (5, 1942)

Richter, Curt P., Ph.D. Phipps Psychiatric Clinic, The Johns Hopkins Hospital, Baltimore, Md. *Associate Professor of Psycho-biology, Johns Hopkins University.* (1, 1924)

Richter, Maurice N., M.D. 303 E. 20th St., New York City. *Professor of Pathology, Columbia University, New York Post-Graduate Medical School; Director, Department of Pathology, New York Post-Graduate Medical School and Hospital.* (4, 1931)

Ricketts, Henry T., M.D. University of Chicago, Chicago, Ill. *Assistant Professor of Medicine.* (1, 1940)

Riddle, Oscar, Ph.D. Cold Spring Harbor, L. I., N. Y. *Resident Staff, Carnegie Station for Experimental Evolution; Member of the National Academy of Sciences.* (1, 1919)

Riegel, Byron, A.M., Ph.D. Department of Chemistry, Northwestern University, Evanston, Ill. *Associate Professor.* (2, 1942)

Riegel, Cecilia, M.S., Ph.D. Room 563, University Hospital, Philadelphia, Pa. *Research Associate, Department of Research S y, University of Pennsylvania School e.* (2, 1938)

Ries, Ferd A., M.D i- more, Md. *I Hopkins U*

Rigdon, R. H., M.D. Pathological Institute, The University of Tennessee, Memphis. *Associate Professor of Pathology.* (4, 1941)

Riggs, Lloyd K., Ph.D. % Kraft Cheese Co., 500 Peshtigo Court, Chicago, Ill. *Director of Research.* (2, 1929)

Rinehart, James F., M.D. University of California Medical School, Parnassus and Third Aves., San Francisco. *Professor of Pathology and Medicine.* (4, 1933)

Ring, Gordon C., M.A., Ph.D. Station Hospital No. 2, Fort Huachuca, Ariz. *Captain, Medical Corps.* (1, 1933)

Rioch, David McKenzie, M.D. Washington University School of Medicine, St. Louis, Mo. *Professor of Neurology and Head of the Department of Neuropsychiatry.* (1, 1931)

Rittenberg, David, Ph.D. 630 W. 168th St., New York City. *Assistant Professor, College of Physicians and Surgeons, Columbia University.* (2, 1939)

Ritzman, E. G., A.M., Science (hon.). University of New Hampshire, Durham. *Research Professor.* (5, 1933)

Rivers, T. M., M.D., Sc.D. The Hospital of the Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Director of the Hospital; Member of the National Academy of Sciences.* (4, 1925; 6, 1921)

Robb, Jane Sands, Sc.D., M.D. College of Medicine, Syracuse University, 761 Irving Ave., Syracuse, N. Y. *Associate Professor of Pharmacology.* (1, 1924)

Robbins, Benjamin Howard, M.S., M.D. Vanderbilt Univ. School of Medicine, Nashville, Tenn. *Associate Professor of Pharmacology.* (3, 1936)

Roberts, Edward F., M.D., Ph.D. Room 103, Army Medical Center, Washington, D. C. *Capt., M. C.* (6, 1932)

Roberts, Lydia J., Ph.D. University of Chicago, Chicago, Ill. *Professor and Chairman of Department of Home Economics.* (5, 1933)

Robertson, Elizabeth Chant, M.D., M.A., Ph.D. University of Toronto, Toronto, Canada. *Research Fellow in Paediatrics.* (5, 1939)

Robertson, Oswald H., M.D. University of Chicago, Chicago, Ill. *Professor of Medicine.* (4, 1932)

Robinson, Charles Summers, Ph.D. Medical School, Vanderbilt University, Nashville, Tenn. *Professor of Biochemistry.* (2, 1925)

Robinson, Elliott S., M.D., Ph.D. 5 Oakwood Terrace, Newton Centre, Mass. *Lieutenant Colonel, M. C., U. S. A.* (6, 1935)

Robinson, G. Canby, M.D., Sc.D., LL.D. Johns Hopkins Hospital, Baltimore, Md. *Lecturer in Medicine, Johns Hopkins University.* (1, 1912; 3, 1921)

Robinson, George Henry, Ph.D. 320 E. North Ave., N. S., Pittsburgh, Pa. *Bacteriologist, Wm. H. Singer Research Laboratory and Allegheny General Hospital; Lecturer in Bacteriology, University of Pittsburgh School of Medicine.* (4, 1930)

Robinson, Howard West, Ph.D. 1208 S. Ruby St., Philadelphia, Pa. *Research Chemist, Department of Pediatrics, Temple University School of Medicine.* (2, 1929)

Robinson, Sid, Ph.D. Fatigue Laboratory, Morgan Hall, Soldiers Field Station, Boston, Mass. (1, 1941)

Robscheit-Robbins, F. S., Ph.D. University of Rochester School of Medicine and Dentistry, Rochester, N. Y. *Associate in Pathology.* (1, 1925; 4, 1930)

Rodbard, Simon, Ph.D. Fifth Altitude Training Unit, Davis Monthan Field, Tucson, Ariz. *2nd. Lt. Air Corps.* (1, 1942)

Roe, Joseph Hyram, M.A., Ph.D. George Washington University School of Medicine, Washington, D. C. *Professor of Biochemistry.* (2, 1927; 5, 1933)

Roeder, Kenneth D., M.A. Tufts College, Medford, Mass. *Assistant Professor of Biology.* (1, 1942)

Roepke, Martin Henry, Ph.D. University Farm, St. Paul, Minn. *Professor, Veterinary Medicine.* (3, 1937)

Rogers, Charles G., A.M., Ph.D., Sc.D. Oberlin College, Oberlin, O. *Professor of Comparative Physiology.* (1, 1911)

Rogers, Fred T., A.M., Ph.D., M.D. Dallas Medical and Surgical Clinic, Dallas, Texas. (1, 1917)

Rogoff, Julius M., Ph.G., M.D., Sc.D. School of Medicine, University of Pittsburgh, Pittsburgh, Pa. *Professor of Endocrinology.* (1, 1916; 3, 1916)

Ronzoni, Ethel, M.A., Ph.D. Washington University Medical School, St. Louis 4, Mo. *Assistant Professor of Biological Chemistry.* (2, 1923)

Root, Howard F., M.D. 44 Dwight St., Brookline, Mass. *Instructor in Medicine, Harvard Medical School.* (5, 1933)

Root, Walter S., Ph.D. College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City. *Associate Professor of Physiology.* (1, 1932)

Rosahn, Paul D., M.D. Yale University School of Medicine, New Haven, Conn. *Assistant Clinical Professor of Pathology.* (4, 1934)

Rose, Anton Richard, M.S., Ph.D. Box 176, Edgewater, N. J. *Biochemist, Prudential Insurance Company of America.* (2, 1916; 5, 1933)

Rose, William C., Ph.D. University of Illinois, Urbana. *Professor of Biochemistry; Member, National Academy of Sciences.* (2, 1912; 5, 1933)

Rosenblueth, Arturo, M.D. Harvard Medical School, Boston, Mass. *Assistant Professor of Physiology.* (1, 1932)

Rosenfeld, Morris, M.D. Johns Hopkins School of Medicine, Baltimore, Md. *Associate in Pharmacology and Experimental Therapeutics.* (3, 1934)

Rosenow, Edward C., M.D., hon. LL.D. and D.Sc. Mayo Clinic, Rochester, Minn. *Professor of Experimental Bacteriology, Mayo Foundation, University of Minnesota.* (4, prior to 1920; (6, 1915)

Rosenthal, Sanford M., M.D. National Institute of Health, Washington, D. C. *Senior Pharmacologist, U. S. Public Health Service.* (3, 1925)

Rosenthal, S. R., M.D., Ph.D. University of Illinois College of Medicine, Chicago. *Assistant Professor of Bacteriology and Public Health in Dept. of Pathology and Bacteriology; Director, Tice Laboratory for B. C. G. Vaccination against Tuberculosis, Municipal Tuberculosis Sanatorium.* (4, 1941)

Ross, Joseph F., M.D. The Robert Dawson Evans Memorial, 65 E. Newton St., Boston, Mass. *Assistant Professor of Medicine, Boston University School of Medicine; Associate Member, Robert Dawson Evans Memorial.* (4, 1941)

Ross, William F., Ph.D. Research Laboratory, Shell Oil Company, Wood River, Ill. *Chief Research Chemist.* (2, 1940)

Roth, George B., M.D. 1335 H St., N.W., Washington, D. C. *Professor of Physiology and Pharmacology, George Washington University School of Medicine.* (1, 1914; 3, 1911)

Roth, Grace M., M.S., Ph.D. Mayo Clinic, Rochester, Minn. *Associate in Clinical Physiology.* (1, 1939)

Roth, Paul, M.D. Battle Creek Sanitarium, Battle Creek, Mich. *Director of Physical Therapy.* (1, 1929; 5, 1933)

Rothemund, Paul W. K., Dipl.-Ing., Dr.-Ing. (Munich). Antioch College, Yellow Springs, O. *Associate Professor of Biochemistry, and Research Chemist, The C. F. Kettering Foundation, Antioch College; Associate Professor (Non-resident), Department of Chemistry, Ohio State University.* (2, 1940)

Rous, Peyton, M.D., Sc.D. Rockefeller Institute for Medical Research, York Ave. at 66th St., New York City. *Member; Member of the National Academy of Sciences.* (4, prior to 1920)

Routh, Joseph I., M.S., Ph.D. Chemistry Department, State University of Iowa, Iowa City. *Assistant Professor of Biochemistry.* (2, 1942)

Rowntree, Jennie I., M.S., Ph.D. University of Washington, Seattle. *Professor of Home Economics.* (5, 1933)

Rowntree, L. G., Sc.D., M.D., F.A.C.P. The Touraine, 1520 Spruce St., Philadelphia, Pa. Temp. address: 4701 Connecticut Ave., N. W. Washington, D. C. *Director of the Philadelphia Institute for Medical Research; Research Clinician, Philadelphia General Hospital; Chief Medical Selective Service National Headquarters, Washington, D. C.; Colonel, Medical Research.* (1, 1911; 2, 1910; 3, 1908; 4, prior to 1920)

Rubenstein, Boris B., M.A., M.D., Ph.D. Schick General Hospital, Clinton, Ia. (1, 1931)

Rubin, Morton A., Ph.D. (Capt., Signal Corps, U. S. Army). 720 21st St., South Arlington, Va. *Office of the Chief Signal Officer, Military Personnel Division, Washington, D. C.* (1, 1940)

Ruch, Theodore C., M.A., Ph.D. Yale University School of Medicine, New Haven, Conn. *Assistant Professor of Physiology.* (1, 1933)

Rusch, Harold Paul, M.D. University of Wisconsin, McArdle Memorial Laboratory, Madison. *Associate Professor of Oncology.* (4, 1940)

Russell, Jane A., Ph.D. Yale University School of Medicine, 333 Cedar St., New Haven, Conn. *Instructor in Physiological Chemistry.* (1, 1939)

Russell, Walter C., Ph.D. New Jersey Agricultural Experiment Station and Rutgers University, New Brunswick. *Biochemist in Nutrition and Professor of Agricultural Biochemistry.* (2, 1932; 5, 1933)

Ryan, Andrew Howard, M.D. 210 E. Ohio St., Suite 402, Chicago, Ill. (1, 1912)

Sabin, Florence R., M.D., Sc.D. 1333 E. 10th Ave., Denver, Colo. *Member Emeritus of the Rockefeller Institute; Member of the National Academy of Sciences.* (1, 1923)

Sachs, Ernest, M.D. 97 Arundel Pl., St. Louis, Mo. *Professor of Clinical Neurological Surgery, Washington University Medical School.* (1, 1910)

Sacks, Jacob, Ph.D., M.D. University of Michigan Medical School, Ann Arbor. *Assistant Professor of Pharmacology.* (3, 1933)

Sah, Peter P. T., M.S., Ph.D. Department of Chemistry, Fu Jen University, Peiping, China; *Professor of Chemistry; Lecturer in Pharmacology, Peiping Union Medical College.* (3, 1941)

Sahyun, Melville, A.M., Ph.D. Frederick Stearns & Co., 6533 E. Jefferson St., Detroit, Mich. *Director of Research.* (2, 1932)

Salant, William, M.D. 617 West End Ave., New York City. (1, 1905; 2, 1906; 3, 1908)

Salmon, W. D., A.M. Alabama Polytechnic Institute, Auburn. *Animal Nutritionist.* (2, 1929; 5, 1933)

Salter, William T., M.D. Yale School of Medicine, 333 Cedar St., New Haven, Conn. *Professor of Pharmacology.* (1, 1933; 3, 1942; 5, 1934)

Sampson, John J., M.D. 490 Post St., San Francisco, Calif. *Assistant Clinical Professor of Medicine, University of California Medical School.* (1, 1932)

Sampson, Myra, A.M., Ph.D. Smith College, Northampton, Mass. *Professor and Chairman of Department of Zoology.* (5, 1935)

Samuels, Leo T., Ph.D. 311 Millard Hall, University of Minnesota, Minneapolis. *Associate Professor of Physiological Chemistry.* (2, 1941; 3, 1937)

Sandels, Margaret R., A.M., Ph.D. Florida State College for Women, Tallahassee. *Dean of School of Home Economics; Professor of Nutrition.* (5, 1933)

Sandiford, Irene, Ph.D. Billings Hospital, University of Chicago, Chicago, Ill. *Assistant Professor of Medicine.* (2, 1925; 5, 1933)

Sanford, Arthur H., A.M., M.D. Clinical Laboratories, Mayo Clinic, Rochester, Minn. *Head, Division of Clinical Laboratories.* (6, 1920)

Santos, Francisco O., M.S., Ph.D. University of the Philippines, Los Banos, Laguna. *Professor and Head of Department of Agricultural Chemistry, College of Agriculture.* (5, 1936)

Saphir, Otto, M.D. Michael Reese Hospital, 29th St. and Ellis Ave., Chicago 16, Ill. *Pathologist, Michael Reese Hospital; Professor of Pathology, University of Illinois Medical School.* (4, 1927)

Sappington, Samuel W., M.D., D.Sc. 235 N. 15th St., Philadelphia, Pa. *Professor of Pathology, Hahnemann Hospital.* (6, 1913)

Saslow, George, Ph.D., M.D. Department of Neuropsychiatry, Washington University Medical School, 640 South Kingshighway, St. Louis, Mo. *Instructor in Psychiatry.* (1, 1936)

Satterfield, George H., A.M. University of North Carolina, Raleigh. *Professor of Biochemistry.* (5, 1941)

Saul, Leon Joseph, M.A., M.D. U. S. Naval Training Station, Farragut, Idaho. (1, 1933)

Saunders, Felix, Ph.D. 231 Playa del Sur, La Jolla, Calif. (2, 1938)

Sawyer, Margaret E. MacKay, M.A., Ph.D. 183 University Ave., Kingston, Ontario, Canada. (1, 1935)

Sawyer, Wilbur A., M.D. 29 Ferndale Drive, Hastings-on-Hudson, N. Y. *Director, International Health Division, Rockefeller Foundation.* (4, 1930; 6, 1935)

Scammon, Richard E., M.A., Ph.D. 172 S. E. Bedford St., Minneapolis, Minn. *Distinguished Service Professor in the Graduate School, University of Minnesota.* (1, 1923)

Scharles, Frederick H., M.D. 1405 Bryant Bldg., Kansas City, Mo. (5, 1935)

Schattenberg, Herbert John, M.S., M.D. Bureau of Laboratories, Medical and Surgical Memorial Hospital, 205 Camden St., San Antonio, Texas. *Director.* (4, 1940)

Schenken, John R., M.D. Louisiana State University School of Medicine, New Orleans. *Professor of Pathology and Bacteriology.* (4, 1942)

Scherp, Henry W., M.S., Ph.D. University of Rochester Medical School, 260 Crittenden Blvd., Rochester, N. Y. *Assistant Professor of Immunochemistry.* (6, 1940)

Schick, Bela, M.D. 17 E. 84th St., New York City. *Pediatrician, Mt. Sinai Hospital.* (6, 1924)

Schiffrin, Milton J.,* M.S., Ph.D. 38th Altitude Training Unit, A.P.O. 825, Postmaster, New Orleans, La. *Lieutenant; Director, Altitude Training Unit.* (1, 1943)

Schlenk, Fritz, Ph.D. University of Texas Medical School, Galveston. *Assistant Professor.* (2, 1942)

Schlesinger, M. J., Ph.D., M.D. Beth Israel Hospital, 330 Brookline Ave., Boston, Mass. *Associate in Pathology, Harvard Medical School; Director of Pathology, Beth Israel Hospital.* (4, 1942; 6, 1921)

Schlomovitz, Benjamin H., M.D. 1210 Majestic Bldg., 231 W. Wisconsin Ave., Milwaukee, Wis. *Director, Clinical and Research Laboratory, Veterans Administration Hospital, Wood, Wisconsin.* (1, 1919)

Schlutz, F. W., M.D., M.S. 950 E. 59th St., Chicago 37, Ill. *Chairman of Pediatric Department and Bobs Roberts Hospital, University of Chicago.* (2, 1924; 5, 1936)

Schmeisser, Harry C., M.D. University of Tennessee, Memphis. *Professor of Pathology and Bacteriology.* (4, 1937)

Schmidt, Carl F., M.D. Medical School, University of Pennsylvania, Philadelphia. *Professor of Pharmacology.* (1, 1929; 3, 1924)

Schmidt, Carl L. A., M.S., Ph.D. University of California, Berkeley. *Professor of Biochemistry; Chairman of Division; Dean of the College of Pharmacy.* (2, 1919)

Schmidt, C. Robert, Ph.D., M.D. Hertzler Clinic, Halstead, Kan. *Resident Surgeon.* (1, 1940)

Schmidt, Gerhard, M.D. Boston Dispensary, 25 Bennett St., Boston, Mass. (2, 1939)

Schmidt, Leon H., M.S., Ph.D. Christ Hospital, Institute for Medical Research, Cincinnati, O. *Director of Research; Assistant Professor of Biological Chemistry, College of Medicine, University of Cincinnati.* (2, 1936)

Schmitt, Francis Otto, Ph.D. Dept. of Biology and Public Health, Massachusetts Institute of Technology, Cambridge. *Professor of Biology.* (1, 1930)

Schnedorf, Jerome G., M.D., Ph.D. The University of Kansas School of Medicine, Kansas City. *Associate in Surgery.* (1, 1941)

Schneider, Edward C., Ph.D., Sc.D. 25 Gordon Place, Middletown, Conn. *Professor of Biology, Wesleyan University.* (1, 1912; 2, 1912).

Schoenbach, Emanuel B., M.D. Meningococcal Meningitis Commission, Johns Hopkins School of Hygiene, 615 N. Wolfe St., Baltimore, Md. (6, 1941)

Schoepfle, Gordon M., A.M., Ph.D.* Washington University, School of Medicine, St. Louis, Mo. *Instructor in Physiology.* (1, 1913)

Schradieck, Constant E., M.D. 65 Hazard Ave., Providence, R. I. *Director, Pathological Department, Homeopathic Hospital of Rhode Island.* (6, 1921)

Schreiner, Oswald, M.S., Ph.D. Bureau of Plant Industry, U. S. Department of Agriculture, Washington 25, D. C. *Chief, Division of Soil Fertility Investigations.* (2, 1908)

Schroeder, E. F., M.S., Ph.D. G. D. Searle & Co., P. O. Box 5110, Chicago 80, Ill. *Research Biochemist.* (2, 1938)

Schuck, Cecelia, Ph.D. Purdue University, Lafayette, Ind. *Professor of Nutrition, Department of Home Economics.* (5, 1941)

Schultz, Edwin William, M.D. 743 Cooksey Lane, Stanford University, Calif. *Professor of Bacteriology and Experimental Pathology.* (4, 1927; 6, 1928)

Schultz, Mark P., A.M., M.D. National Institute of Health, Bethesda, Md. *Surgeon, U. S. Public Health Service.* (6, 1933)

Schultz, W. H., Ph.D. Greenspring Ave. & Taney Rd., Baltimore, Md. (1, 1907; 3, 1909)

Schultze, Max O., Ph.D. Department of Chemistry, University of Pittsburgh, Pittsburgh, Pa. *Research Fellow, Buhl Foundation.* (2, 1938)

Schwartze, Erich W., M.D. 1225 Talbert St., S. E., Washington, D. C. (3, 1920)

Scott, David Alymer, M.A., Ph.D. Connaught Laboratories, University of Toronto, Toronto 5, Ontario, Canada. *Senior Research Chemist.* (2, 1935)

Scott, Ernest L., Ph.D. 64 South St., Bogota, N.J. *Associate Professor of Physiology, Emeritus, Columbia University.* (1, 1914; 2, 1915)

Scott, Frederick Hughes, Ph.D., Sc.D., M.B. University of Minnesota, Minneapolis. *Professor of Physiology.* (1, 1908; 2, 1909)

Scott, John C., Ph.D. Hahnemann Medical College, Philadelphia, Pa. *Professor of Physiology and Head of the Department.* (1, 1936)

Scott, R. W., A.M., M.D. City Hospital, Cleveland, O. *Professor of Clinical Medicine, Western Reserve University; Physician-in-chief, Cleveland City Hospital.* (1, 1917; 3, 1917)

Scott, V. Brown, Ph.D., M.D. Inlow Clinic, Shelbyville, Ind. *Internist, Fellow of Inlow Clinic.* (1, 1911)

Scott, W. J. Merle, M.D. University of Rochester Medical School, Rochester, N. Y. *Associate Professor of Surgery.* (4, 1925)

Scott, W. W., M.D.* University Clinics, University of Chicago, Chicago, Ill. *Instructor in Surgery.* (1, 1913)

Scudi, John Vincent, Ph.D. Merck & Co., Inc., Rahway, N. J. *Research Chemist.* (2, 1912)

Seager, Lloyd D., M.S., M.D. University of Tennessee Medical School, 870 Union Ave., Memphis. *Instructor in Pharmacology.* (3, 1939)

Sealock, Robert R., Ph.D. Department of Vital Economics, University of Rochester Medical School, Crittenden Blvd., Rochester, N. Y. *Assistant Professor of Physiological Chemistry.* (2, 1940; 5, 1941)

Seastone, C. V., Jr., M.D. University of Wisconsin Medical School, Madison. *Associate Professor of Medical Bacteriology.* (6, 1939)

Sebrell, W. H., Jr., M.D. National Institute of Health, Bethesda, Md. *Chief, Division of Chemotherapy.* (2, 1938; 5, 1937)

Seecof, David P., M.D. 1970 Daly Ave., Bronx, New York City. (4, 1927)

Seegal, David, M.D. Welfare Island, New York City. *Director, Research and Clinical Service, First Division, Welfare Hospital; Associate Professor of Medicine, Columbia University.* (6, 1930)

Seegers, Walter H., Ph.D. Research and Biological Laboratories, Parke Davis & Co., Detroit, Mich. *Research Biochemist.* (2, 1941)

Seevers, Maurice Harrison, Ph.D., M.D. University of Michigan School of Medicine, Ann Arbor. *Professor of Pharmacology and Chairman of the Department.* (1, 1933; 3, 1930)

Seibert, Florence B., Ph.D., Sc.D., LL.D. Henry Phipps Institute, University of Pennsylvania, 7th and Lombard Sts., Philadelphia. *Associate Professor of Biochemistry.* (2, 1925)

Seidell, Atherton, M.S., Ph.D. 2301 Connecticut Ave., Washington, D. C. *Special Expert, National Institute of Health.* (2, 1924)

Seifter, Joseph, M.D. 2109 Adelbert Rd., Cleveland, O. *Assistant Professor of Pharmacology, Western Reserve University.* (3, 1940)

Selle, Wilber Arthur, Ph.D. Medical School, University of Texas, Galveston. *Associate Professor of Physiology.* (1, 1938)

Selye, Hans, M.D., Ph.D. Medical Building, McGill University, Montreal, Que., Canada. *Assistant Professor of Anatomy.* (1, 1934)

Sendroy, Julius, Jr., M.A., Ph.D. Mercy Hospital, 2537 Prairie Ave., Chicago, Ill. *Professor of Chemistry and Cha[illegible] of the Dep[illegible]ent of*

Experimental Medicine, Loyola University. (2, 1928)

Sevag, M. G., Ph.D. Department of Bacteriology, University of Pennsylvania School of Medicine, Philadelphia. *Assistant Professor of Biochemistry in Bacteriology.* (6, 1941)

Sevringhaus, Elmer L., M.A., M.D. Wisconsin General Hospital, Madison. *Professor of Medicine, University of Wisconsin; Consultant in Clinical Chemistry, Wisconsin Psychiatric Institute; Chemist to Wisconsin General Hospital.* (2, 1923; 5, 1939)

Shaffer, Morris F., D. Phil. Department of Pathology and Bacteriology, School of Medicine, Tulane University of Louisiana, New Orleans. *Associate Professor.* (4, 1939; 6, 1937).

Shaffer, Philip A., Ph.D. Washington University Medical School, St. Louis 4, Mo. *Professor of Biological Chemistry and Dean of the School of Medicine; Member, National Academy of Sciences.* (1, 1906; 2, 1906; 5, 1935)

Shannon, James A., M.D., Ph.D. Welfare Hospital, Welfare Island, New York City. *Director of Research Service, Third (New York University) Medical Division, Welfare Hospital, Department of Medicine, New York University College of Medicine.* (1, 1933)

Shapiro, Herbert, A.M., Ph.D. Hahnemann Medical College, Philadelphia, Pa. *Instructor in Physiology,* Radiation Laboratory, M.I.T., Cambridge, Mass. *Staff Member.* (1, 1937)

Sharpless, George R., D.Sc. Henry Ford Hospital, Detroit, Mich. *Associate in Nutrition Research.* (5, 1942)

Shaw, Myrtle, M.S., Ph.D. 11 S. Lake Ave., Albany, N. Y. *Senior Bacteriologist, Division of Laboratories and Research, New York State Department of Health.* (6, 1937)

Shear, Murray, J., Jr., Ph.D. National Cancer Institute, Bethesda, Md. *Principal Biochemist.* (2, 1930)

Sheard, Charles, A.M., Ph.D. Mayo Foundation, Rochester, Minn. *Chief of the Division of Physics and Biophysical Research and Professor of Physiological Optics and Biophysics, University of Minnesota.* (1, 1925)

Sheehan, Donal, M.D., D.Sc. New York University College of Medicine, First Ave., New York City. *Professor of Anatomy and Director of Anatomical Laboratories.* (1, 1938)

Sheppard, Fay, M.S. University of Oklahoma Medical School, Oklahoma City. *Instructor in Biochemistry.* (2, 1936)

Sherman, Henry C., A.M., Ph.D., Sc.D. Columbia University, New York City. *Mitchell Professor of Chemistry and Executive Officer of the Department of Chemistry; Member, National Academy of Sciences.* (1, 1923; 2,1906; 5, 1933)

Sherwin, Carl Paxson, Sc.D., M.D., Dr.P.H., LL.D. 40 E. 61st St., New York City. *Director of Metabolic Service, St. Vincent's Hospital; Associate Physician, French Hospital.* (1, 1919; 2, 1917)

Sherwood, Noble P., Ph.D., M.D. 1801 Indiana St., Lawrence, Kan. *Professor of Bacteriology, University of Kansas.* (6, 1928)

Sherwood, Thomas Cecil, M.A., Ph.D. 2639 Napoleon Ave., New Orleans, La. *House Physician, Southern Baptist Hospital.* (1, 1938)

Shimkin, Michael Boris, M.D. U. S. Public Health Service, National Cancer Institute, Bethesda, Md. *Passed Assistant Surgeon.* (4, 1940)

Shlaer, Simon, M.A., Ph.D. Columbia University, New York City. *Research Associate in Biophysics.* (1, 1938)

Shock, Nathan W., Ph.D. Unit on Gerontology, U. S. Public Health Service, Baltimore City Hospitals, Baltimore, Md. *Senior Psychophysiologist, U. S. Public Health Service, National Institute of Health, Bethesda, Md.* (1, 1942)

Shoemaker, Harold A., M.S., Ph.D. University of Oklahoma School of Medicine, Oklahoma City. *Assistant Dean; Professor of Pharmacology.* (3, 1941)

Shohl, Alfred T., M.D. 300 Longwood Ave., Boston, Mass. *Research Associate in Pediatrics, Harvard Medical School.* (2, 1922; 5, 1933)

Shope, Richard E., M.D. Department of Animal and Plant Pathology, The Rockefeller Institute, Princeton, N. J. *Member.* (4, 1934)

Shorr, Ephraim, M.D. The New York Hospital, 525 East 68th St., New York City. *Assistant Professor of Medicine, Cornell University Medical College; Assistant Attending Physician, The New York Hospital.* (1, 1931; 3, 1942)

Shwartzman, Gregory, M.D. 230 E. 50th St., New York City. *Head of Department of Bacteriology, Mount Sinai Hospital; Clinical Professor of Bacteriology, Columbia University.* (4, 1929; 6, 1930)

Sichel, F. J. M., Sc.M., Ph.D. College of Medicine, University of Vermont, Burlington. *Instructor in Physiology.* (1, 1939)

Sickles, Grace M., B.A. 2201 Twelfth St., Troy, N. Y. *Associate Bacteriologist, Division of Laboratories and Research, New York State Department of Health.* (6, 1932)

Sickles, Gretchen R., A.B. Division of Laboratories and Research, New York State Department of Health, Albany, N. Y. *Assistant Bacteriologist.* (6, 1937)

Siebert, Walter J., M.D. DePaul Hospital, St. Louis, Mo. *Director of Laboratories and Pathologist of DePaul and Lutheran Hospitals, St.*

Louis, and of St. Joseph Hospital, Alton, Ill. (4, 1932)

Silvette, Herbert, M.S., Ph.D. University of Virginia Medical School, University. *Assistant Professor of Pharmacology.* (1, 1933; 3, 1940)

Simon, Frank A., M.D. 812 Heyburn Bldg., Louisville, Ky. (6, 1934)

Simonds, James P., Ph.D., M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Professor of Pathology.* (4, prior to 1920)

Simonson, Ernst, M.D. Mount Sinai Hospital, 12th and Kilbourn Ave., Milwaukee, Wis. *Research Fellow.* (1, 1941)

Sinclair, Robert Gordon, Ph.D. Queen's University, Kingston, Ont., Canada. *Professor of Biochemistry.* (2, 1931)

Slaughter, Donald, M.D. Medical Department, Southwestern Medical Foundation, 3705 Maple Ave., Dallas, Texas. *Acting Dean and Professor of Pharmacology and Physiology.* (3, 1938)

Slonaker, James R., Ph.D. 334 Kingsley Ave., Palo Alto, Calif. *Professor of Physiology, Leland Stanford Junior University.* (1, 1917)

Smadel, Joseph Edwin, M.D. c/o Dr. Elizabeth M. Smadel, Group B, Camp Detrick, Frederick, Md. (4, 1940; 6, 1937)

Small, James C., M.D. 133 S. 36th St., Philadelphia, Pa. *Instructor in Medicine, Graduate School of Medicine, University of Pennsylvania.* (4, 1927)

Smetana, Hans, M.D. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Assistant Professor of Pathology.* (4, 1934)

Smith, Arthur H., M.S., Ph.D. Wayne University College of Medicine, Detroit 26, Mich. *Professor of Physiological Chemistry.* (1, 1923; 2, 1921; 5, 1933)

Smith, Austin Edward, M.D., C.M., M.Sc.(Med.). American Medical Association, 535 N. Dearborn St., Chicago, Ill. *Acting Secretary of the Council on Pharmacy and Chemistry, American Medical Association; Research Associate (Instructor) Dept. of Pharmacology, University of Chicago.* (3, 1942)

Smith, Clarence A., M.S., Ph.D. Standard Brands, Inc., 595 Madison Ave., New York City. *Technical Director, Special Products Department.* (1, 1921)

Smith, David T. Duke Hospital, Durham, N. C. (5, 1943)

Smith, Dietrich Conrad, A.M., Ph.D. University of Maryland School of Medicine, Lombard and Greene Sts., Baltimore. *Associate Professor of Physiology.* (1, 1937)

Smith, Elinor Van Dorn, Ph.D. 5 Middle St., Hadley, Mass. *Assistant Professor of Bacteriology, Smith College.* (6, 1940)

Smith, Elizabeth R. B., Ph.D. % Capt. Paul K. Smith, School of Aviation Medicine, Randolph Field, Texas. (2, 1938)

Smith, Erma A., A.M., Ph.D., M.D. Iowa State College, Ames. *Associate Professor of Physiology.* (1, 1928)

Smith, Fred M., M.D. State University of Iowa, Iowa City. *Professor of the Theory and Practice of Medicine and Head of the Department.* (1, 1925)

Smith, George H., M.A., Ph.D., M.A.(hon.), Sc.D. School of Medicine, Yale University, New Haven, Conn. *Professor of Immunology and Assistant Dean; Chairman, Department of Bacteriology, Yale University.* (6, 1918)

Smith, H. P., M.S., M.D. College of Medicine, State University of Iowa, Iowa City. *Professor of Pathology.* (1, 1937; 4, 1925)

Smith, Homer W., M.S., Sc.D. 477 First Ave., New York City. *Professor of Physiology, New York University College of Medicine.* (1, 1923; 2, 1930)

Smith, Lawrence Weld, M.D. Temple University School of Medicine, N. Broad St., Philadelphia, Pa. *Professor and Head of Department of Pathology; Director of Laboratories, Temple University Hospital.* (4, 1927)

Smith, Lee Irvin, A.M., Ph.D. School of Chemistry, University of Minnesota, Minneapolis. *Professor and Chief, Division of Organic Chemistry.* (2, 1942)

Smith, Margaret Cammack, A.M., Ph.D. University of Arizona, Tucson. *Professor of Nutrition; Nutrition Chemist, Agricultural Experiment Station, School of Home Economics.* (2, 1935; 5, 1933)

Smith, Maurice I., M.D. National Institute of Health, Bethesda, Md. *Principal Pharmacologist., U. S. Public Health Service.* (1, 1920; 3, 1916)

Smith, Paul Kenneth, Ph.D. School of Aviation Medicine, Randolph Field, Texas. *Director, Laboratory of Pharmacology. Captain, U. S. Air Corps.* (2, 1937; 3, 1937)

Smith, Paul W., M.S., Ph.D. School of Medicine, University of Oklahoma, 801 E. 13th St., Oklahoma City. *Assistant Professor of Pharmacology.* (1, 1933)

Smith, Philip Edward, M.S., Ph.D. 630 W. 168th St., New York City. *Professor of Anatomy, Columbia University; Member of the National Academy of Sciences.* (1, 1923)

Smith, Ralph G., M.D., Ph.D. Tulane University, Station 20, New Orleans, La. *Professor of Pharmacology.* (3, 1929)

Smith, Susan Gower, M.A. Duke University, Durham, N. C. *Associate, Department of Medicine and Nutrition, School of Medicine.* (5, 1939)

Smith, Sybil L., A.M. Principal Experiment Station Administrator, Office of Experiment Stations, U.S.D.A., Washington, D. C. (5, 1940)

Smith, Wilbur Kenneth, M.D. University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y. *Associate Professor of Anatomy.* (1, 1939)

Smith, Willie W., M.A., Ph.D. 4710 Edgmoor Lane, Bethesda, Md. *Alfred I. du Pont Institute of the Nemours Foundation. Wilmington, Del.* (1, 1941)

Smithburn, Kenneth C., M.D. Yellow Fever Research Institute, P. O. Box 49, Entebee, Uganda, British East Africa. *Staff Member, International Health Division of The Rockefeller Foundation.* (6, 1937)

Smythe, C. V., M.S., Ph.D. 5000 Richmond St., Philadelphia, Pa. *Head of Biochemistry, Rohm & Haas Company.* (2, 1934)

Snell, Albert M., M.D. Mayo Clinic, Rochester, Minn. *Head of Section on Medicine at Mayo Clinic; Professor in Medicine, Mayo Foundation Graduate School, University of Minnesota.* (4, 1930)

Snell, Esmond E., M.A., Ph.D. Department of Chemistry, University of Texas, Austin. *Assistant Professor of Chemistry and Research Biochemist.* (2, 1942)

Snyder, Charles D., M.S., Ph.D. Johns Hopkins University School of Medicine, Baltimore, Md. *Professor Emeritus of Experimental Physiology.* (1, 1907)

Snyder, Franklin Faust, M.D. University of Chicago, Ill. *Associate, Department of Obstetrics.* (1, 1936)

Sobel, Albert E., Ch.E., M.A., Ph.D. Jewish Hospital of Brooklyn, Prospect Place and Classon Ave., Brooklyn, N. Y. *Director of Chemical Laboratories; Lecturer, Division of Graduate Studies, Brooklyn College.* (2, 1939)

Sobotka, Harry H., Ph.D. Mount Sinai Hospital, Fifth Ave. and 100th St., New York City. *Head, Department of Chemistry.* (2, 1932; 5, 1933)

Solandt, Donald Young, M.A., M.D., Ph.D. University of Toronto, Toronto, Ont., Canada. *Associate Professor of Physiology; Head of the Department of Physiological Hygiene.* (1, 1937)

Soley, Mayo H., M.D.* University of California Medical School, The Medical Center, San Francisco. *Associate Professor of Medicine and Lecturer in Pharmacology.* (1, 1943)

Sollmann, Torald, M.D., Sc.D. School of Medicine, Western Reserve University, 2109 Adelbert Rd., Cleveland, O. *Dean and Professor of Pharmacology and Materia Medica.* (1, 1902; 2, 1906; 3, 1908)

Somogyi, Michael, Ph.D. 216 S. Kingshighway, St. Louis, Mo. *Biochemist, Jewish Hospital of St. Louis.* (2, 1927)

Soskin, Samuel, M.D., M.A., Ph.D. Michael Reese Hospital, Chicago, Ill. *Director of Metabolic and Endocrine Research; Professoral Lecturer in Physiology, University of Chicago.* (1, 1930; 5, 1933)

Soule, Malcolm H., Sc.D., LL.D. University of Michigan, Ann Arbor. *Professor of Bacteriology, Director of the Hygienic Laboratory and Chairman of the Department of Bacteriology.* (4, 1927; 6, 1925)

Spain, Will C., M.D. 116 E. 53rd St., New York City. *Clinical Professor of Medicine, Post-Graduate Medical School, Columbia University.* (6, 1923)

Spealman, C. R., M.A., Ph.D. National Naval Medical Center, Bethesda, Md. (1, 1940)

Specht, Heinz, Ph.D. National Institute of Health, Rockville Pike, Bethesda, Md. *Associate Research Physiologist.* (1, 1941)

Spencer, Henry James, M.A., M.D. Bellevue Hospital, 24 W. 10th St., New York City. *Director Second Medical Division. Associate Professor of Clinical Medicine, Cornell University Medical College.* (5, 1935)

Sperry, Warren M., M.S., Ph.D. 722 W. 168th St., New York City. *Principal Research Neurochemist, New York State Psychiatric Institute and Hospital; Assistant Professor of Biological Chemistry, College of Physicians and Surgeons, Columbia University.* (2, 1929; 5, 1933)

Spiegel, Ernest A., M.D. Temple University School of Medicine, Broad and Ontario Sts., Philadelphia, Pa. *Professor of Experimental Neurology.* (1, 1936)

Spiegel-Adolf, Mona, M.D. Temple University School of Medicine, Broad St. at Ontario Ave., Philadelphia, Pa. *Professor and Head of Department of Colloid Chemistry.* (2, 1933)

Spies, Tom D., M.D. Feb.-Nov. Hillman Hospital, Birmingham, Ala. Nov.-Feb. General Hospital, Cincinnati, O. *Associate Professor of Medicine, Univ. of Cincinnati College of Medicine. Visiting Professor of Medical Research, Univ. of Alabama School of Medicine. Professor of Medical Research, Univ. of Texas School of Medicine. Director, Nutrition Clinic, Hillman Hospital, Birmingham, Ala.* (3, 1941; 4, 1940; 5, 1938)

Spink, Wesley W., M.D. University of Minnesota Hospital, Minneapolis. *Associate Professor of Medicine, University of Minnesota Medical School.* (3, 1940; 4, 1940; 6, 1940)

Spohn, Adelaide, M.S., Ph.D. Elizabeth McCormick Memorial Fund, 848 N. Dearborn St., Chicago, Ill. (5, 1933)

Sproul, Edith E., M.D. Columbia University, College of Physicians and Surgeons, New York City. *Assistant Professor of Pathology.* (4, 1941)

Sprunt, Douglas H., M.D., M.S. Box 3611, Duke Hospital, Durham, N. C. *Associate Professor of Pathology.* (4, 1931; 6, 1936)

Stadie, William C., M.D. 821 Maloney Clinic, 36th and Spruce Sts., Philadelphia, Pa. *Professor of Research Medicine, University of Pennsylvania.* (2, 1922)

Stainsby, Wendell J., M.D., C.M. Geisinger Memorial Hospital, Danville, Pa. *Chief Physician.* (6, 1930)

Stanley, Wendell M., M.S., Ph.D., Sc.D. Rockefeller Institute for Medical Research, Princeton, N. J. *Member; Member, National Academy of Sciences.* (2, 1936)

Stannard, James Newell, Ph.D. National Institute of Health, Division of Industrial Hygiene, Bethesda, Md. *Pharmacologist.* (1, 1938)

Stare, Fredrick J., Ph.D., M.D. Department of Biological Chemistry, Harvard Medical School, Boston, Mass. *Assistant Professor of Nutrition.* (2, 1937; 5, 1942)

Starr, Isaac, M.D. 817 Maloney Clinic, Hospital of the University of Pennsylvania, Philadelphia, Pa. *Hartzell Professor of Research Therapeutics.* (1, 1929; 3, 1942)

Stavraky, George W., M.D., C.M., M.Sc. Medical School, University of Western Ontario, London, Ont., Canada. *Associate Professor of Physiology.* (1, 1937)

Stearns, Genevieve, Ph.D. College of Medicine, State University of Iowa, Iowa City. *Research Professor of Pediatrics.* (2, 1932; 5, 1937)

Steel, Matthew, Ph.D. Long Island College of Medicine, 350 Henry St., Brooklyn, N. Y. *Professor of Biological Chemistry.* (2, 1909)

Steele, J. Murray, M.D. Welfare Hospital, Welfare Island, New York City. *Associate Professor of Medicine, New York University; Director 3rd (New York University) Medical Division of Welfare Hospital.* (1, 1936)

Steenbock, Harry, M.S., Ph.D., Sc.D. University of Wisconsin, Madison. *Professor of Biochemistry.* (2, 1912; 5, 1933)

Steggerda, F. R., M.A., Ph.D. 416 Natural History Building, University of Illinois, Urbana. *Assistant Professor of Physiology.* (1, 1934)

Stehle, Raymond Louis, A.M., Ph.D. Faculty of Medicine, McGill University, Montreal, Canada. *Professor of Pharmacology.* (2, 1920; 3, 1922)

Steigmann, Frederick, M.S., M.D. 348 S. Hamlin Ave., Chicago, Ill. *Associate in Medicine, College of Medicine, University of Illinois; Associate Attending Physician, Cook County Hospital.* (3, 1942)

Steimann, S. E., M.A., Ph.D. 361 Riverway, Boston, Mass. (1, 1939)

Steinbach, H. Burr, M.A., Ph.D. Washington University, St. Louis, Mo. *Associate Professor of Zoology.* (1, 1934)

Steinberg, Bernhard, M.D. Toledo Hospital Institute of Medical Research, Toledo, O. *Director of the Toledo Hospital Institute of Medical Research; Director of Clinical and Morbid Pathological Laboratories, The Toledo Hospital.* (4, 1928)

Steiner, Paul E., M.D. The University of Chicago, Chicago, Ill. *Associate Professor of Pathology.* (4, 1939)

Steinhardt, Jacinto, A.M., Ph.D. 1518 East-West Highway, Silver Spring, Md. *Research Associate, Division of War Research, Columbia University, New York City.* (2, 1939)

Steinhaus, Arthur H., M.S., Ph.D., M.P.E. 5315 Drexel Ave., Chicago, Ill. *Professor of Physiology, George Williams College, Hyde Park.* (1, 1928)

Stekol, Jakob A., M.S., D.Sc. Department of Biochemistry, Vanderbilt University, Nashville, Tenn. *Assistant Professor.* (2, 1936)

Stern, Kurt G., Ph.D. 254 W. 31st St., New York City. *Chief Chemist, Overly Biochemical Research Foundation.* (2, 1938)

Stevens, S. Smith, Ph.D. Emerson Hall, Harvard University, Cambridge, Mass. *Assistant Professor of Psychology.* (1, 1937)

Stewart, Colin C., Ph.D. Dartmouth College, Hanover, N. H. *Brown Professor of Physiology.* (1, 1898)

Stewart, Fred W., M.D. Memorial Hospital, 444 E. 68th St., New York City. *Pathologist; Associate Professor of Surgical Pathology, Cornell Medical School; Pathologist, New York State Department of Public Health, Division of Laboratories and Research.* (4, 1928)

Stewart, Harold L., M.D. The National Cancer Institute, Bethesda, Md. *Senior Pathologist.* (4, 1936)

Stewart, Winifred Bayard, M.D., M.A. 2028 Delancey St., Philadelphia, Pa. *Professor of Neurology, Woman's Medical College of Pennsylvania.* (1, 1941)

Stiebeling, Hazel K., M.A., Ph.D. United States Department of Agriculture, Washington, D. C. *Senior Food Economist, Bureau of Home Economics.* (5, 1933)

Stier, Theodore J. B., Ph.D. Indiana University Medical School, Bloomington. *Associate Professor of Physiology.* (1, 1938)

Still, Eugene U., Ph.D. % Strong Cobb & Co., 2654 Lisbon Rd., Cleveland, O. (1, 1929)

Stillman, Ernest G., M.D. 45 E. 75th St., New York City. (6, 1930)

Stockton, Andrew Benton, M.D. 564 Funston Ave., San Francisco, Calif. *Assistant Clinical Professor of Medicine, Stanford Medical School.* (3, 1931)

Stokstad, E. L. Robert, Ph.D. Lederle Laboratories, Pearl River, N. Y. *Research Chemist.* (5, 1942)

Stoland, O. O., M.S., Ph.D. 1845 Learnard Ave., Lawrence, Kan. *Professor of Physiology and Pharmacology, University of Kansas.* (1, 1913)

Stormont, Robert T., Ph.D. University of Chicago, Chicago, Ill. *Research Assistant in Pharmacology, Otho S. A. Sprague Memorial Institute.* (3, 1941)

Stotz, Elmer H., Ph.D. New York State Agricultural Experiment Station, Geneva, N. Y. *Professor of Chemistry.* (2, 1939)

Stoughton, Roger W., M.S., Ph.D. Mallinckrodt Chemical Works, 3600 N. Second St., St. Louis, Mo. *Research Chemist.* (3, 1939)

Strong, Frank M., M.A., Ph.D. Department of Biochemistry, University of Wisconsin, Madison. *Associate Professor of Biochemistry.* (2, 1941)

Struck, Harold Carl, Ph.D. University of Illinois College of Medicine, 1853 W. Polk St., Chicago. *Assistant Professor of Pharmacology and Therapeutics.* (1, 1940)

Stuart, Charles A., M.Sc., Ph.D. 372 Lloyd Ave., Providence, R. I. *Associate Professor of Biology, Brown University.* (6, 1935)

Sturgis, Cyrus Cressey, M.D. Simpson Memorial Institute, Ann Arbor, Mich. *Director, Thomas Henry Simpson Memorial Institute for Medical Research; Chairman, Department of Medicine, University Hospital, and Professor of Medicine, University of Michigan.* (4, 1927)

SubbaRow, Y., Ph.D. Lederle Laboratories, Pearl River, N. Y. (2, 1939)

Sugg, John Y., Ph.D. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor of Bacteriology and Immunology.* (6, 1938)

Sullivan, Michael Xavier, Ph.D. Chemo-Medical Research Institute, Georgetown University, 37th & O Sts., N. W., Washington, D. C. *Director and Research Professor of Chemistry.* (2, 1909)

Sulzberger, Marion B., M.D. 962 Park Ave., New York City. *Lieutenant Commander, M.C., U.S.N.R., in charge of Dermatology and Syphilology, U. S. Naval Hospital, Brooklyn, N. Y.; Assistant Clinical Professor of Dermatology and Syphilology, Columbia University.* (6, 1936)

Summerson, William H., M.A., Ph.D. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor of Biochemistry.* (2, 1942)

Sumner, James Batcheller, A.M., Ph.D. Dairy Building, Ithaca, N. Y. *Professor of Biochemistry, Cornell University Medical College.* (2, 1919)

Sumwalt, Margaret, M.S., Ph.D. Medical School, University of Pennsylvania, Philadelphia. (1, 1934)

Sunderman, F. William, M.D., Ph.D. University of Pennsylvania, Philadelphia. *Assistant Professor of Research Medicine.* (2, 1931)

Sundstroem, Edward S., M.D. University of California, Berkeley. *Associate Professor of Biochemistry.* (2, 1919)

Sure, Barnett, M.S., Ph.D. University of Arkansas, Fayetteville. *Head of Department and Professor of Agricultural Chemistry.* (2, 1923; 5, 1933)

Sutherland, George F., M.D.C.M., M.Sc. Worcester State Hospital, Worcester, Mass. *Research fellow in Neuropathology, Harvard Medical School; Captain, M.C., Darnall General Hospital, Danville, Ky.* (1, 1939)

Sutton, T. Scott, M.Sc., Ph.D. Ohio State University, Columbus. *Assistant Professor; Associate, Ohio Agricultural Experiment Station, College of Agricutlure.* (5, 1936)

Swain, Robert E., M.S., Ph.D., LL.D. 634 Mirada Ave., Stanford University, Calif. *Professor Emeritus of Chemistry.* (2, 1909)

Swann, Howard G., M.S., Ph.D. Dept. of Pharmacology, University of Texas Medical School, Galveston. *Assistant Professor of Physiology.* (1, 1940)

Swanson, Pearl P., M.S., Ph.D. Iowa State College, Ames. *Professor of Foods and Nutrition, Dept. of Foods and Nutrition.* (5, 1933)

Swanson, William W., M.S., M.D. 2376 E. 71st St., Chicago, Ill. (2, 1938)

Sweeney, H. Morrow, M.S., Ph.D. School of Medical Sciences, University of South Dakota, Vermillion. *Professor of Physiology and Pharmacology and Head of the Department.* (1, 1939)

Sweet, J. E., A.M., M.D., Sc.D. Unadilla, N. Y. *Emeritus Professor of Surgical Research, Cornell Medical College.* (1, 1913)

Swift, Homer, M.D., D.Sc. 888 Park Ave., New York City. *Member, Rockefeller Institute for Medical Research; Physician to The Hospital of The Rockefeller Institute for Medical Research.* (6, 1920)

Swift, Raymond W., M.S., Ph.D. Pennsylvania State College, State College. *Professor, Institute of Animal Nutrition.* (5, 1934)

Swingle, Wilbur Willis, Ph.D. Princeton University, Princeton, N. J. *Professor of Biology.* (1, 1924)

Sykes, Joseph F., M.S.A., Ph.D. Michigan State College, E. Lansing. *Research Assistant and Assistant Professor of Physiology and Pharmacology.* (1, 1942)

Syverton, Jerome T., M.D. The University of Rochester School of Medicine and Dentistry and Strong Memorial Hospital, Rochester, N. Y. *Associate Professor of Bacteriology.* (4, 1940)

Tainter, M. L., M.A., M.D. Winthrop Chemical Company, Rensselaer, N. Y. *Director of Research.* (1, 1929; 3, 1927)

Tait, John, M.D., D.Sc., F.R.S.E., F.R.S.C. McGill University, Montreal, Que., Canada. *Professor of Physiology (Retired).* (1, 1919)

Talbert, George A., Ph.D. University Station, Grand Forks, N. D. *Professor of Physiology and Pharmacology, University of North Dakota.* (1, 1919)

Talbot, Samuel Armstrong, A.M., M.S., Ph.D. Wilmer Institute, Johns Hopkins Hospital, Baltimore, Md. *Instructor in Physiological Optics, Johns Hopkins University.* (1, 1940)

Taliaferro, William H., Ph.D. Department of Bacteriology, University of Chicago, Chicago, Ill. *Eliakim H. Moore Distinguished Service Professor of Parasitology and Dean of the Division of Biological Sciences.* (6, 1930)

Tannenbaum, Albert, M.D. Michael Reese Hospital, 29th St. & Ellis Ave., Chicago, Ill. *Director, Department of Cancer Research.* (4, 1942)

Tashiro, Shiro, Ph.D., M.D. College of Medicine, University of Cincinnati, Cincinnati, O. *Professor of Biochemistry.* (1, 1913; 2, 1913)

Tatum, Arthur L., M.S., Ph.D., M.D. University of Wisconsin, Madison. *Professor of Pharmacology.* (1, 1913; 3, 1919)

Tauber, Henry, Ph.D. Publicker Commercial Alcohol Co., Philadelphia, Pa. *Supervisor of Ethyl Alcohol Fermentation.* (2, 1933)

Taylor, Alonzo E., M.D. General Mills, Inc. 200 Chamber of Commerce, Minneapolis, Minn. *Director of Research. Director Emeritus, Food Research Institute, Stanford University.* (5, 1933)

Taylor, Fred A., Ph.D. 320 E. North Ave., N.S., Pittsburgh, Pa. *Biochemist, Singer Memorial Laboratory.* (2, 1933)

Taylor, Haywood M., M.S., Ph.D. Duke University School of Medicine, Durham, N. C. *Associate Professor of Biochemistry and Toxicology; Toxicologist to Duke Hospital.* (4, 1942)

Taylor, Norman Burke, M.D., F.R.S. (Can.), M.R.C.S. (Eng.), L.R.C.P. (Lon.), F.R.C.S. (Edin.), F.R.C.P. (Can.). University of Toronto, 5, Ontario, Ont., Canada. *Professor of Physiology.* (1, 1922)

Teague, Robert S., M.D., Ph.D. Department of Pharmacology and Physiology, University of Alabama, University. *Instructor in Pharmacology.* (3, 1942)

Templeton, Roy D., B.S. 2010 N. Broadway, Shelbyville, Ill. Loyola University School of Medicine, 706 South Lincoln St., Chicago, Ill. *Associate in Physiology.* (1, 1935)

Ten Broeck, Carl, M.D. The Rockefeller Institute for Medical Research, Department of Animal and Plant Pathology, Princeton, N. J. *Member.* (4, 1932; 6, 1924)

Terplan, Kornel L., M.D. University of Buffalo, School of Medicine, Buffalo, N. Y. *Professor of Pathology and Bacteriology.* (4, 1935)

Thannhauser, S. J., M.D., Ph.D. Tufts College Medical School, 30 Bennet St., Boston, Mass. *Clinical Professor of Medicine; Associate Physician in Chief, Joseph H. Pratt Diagnostic Hospital.* (2, 1937)

Thayer, Sidney Allen, Ph.D. 1402 S. Grand Blvd., St. Louis 4, Mo. *Assistant Professor of Biochemistry, St. Louis University School of Medicine.* (2, 1933)

Theiler, Max, M.D. Rockefeller Foundation, New York City. *Member of Field Staff.* (4, 1938)

Thienes, Clinton H., A.M., M.D., Ph.D. University of Southern California School of Medicine, Los Angeles. *Professor of Pharmacology.* (3, 1928)

Thomas, Arthur W., Ph.D. Columbia University, New York City. *Professor of Chemistry.* (2, 1924)

Thomas, Byron H., M.S., Ph.D. Iowa State College, Ames. *Professor and Head, Animal Chemistry and Nutrition, Iowa Agricultural Experiment Station.* (5, 1933)

Thomas, Caroline Bedell, M.D. The Johns Hopkins Hospital, Baltimore, Md. *Instructor in Medicine, Johns Hopkins University School of Medicine.* (1, 1939)

Thomas, J. Earl, M.S., M.D. Jefferson Medical College, Philadelphia, Pa. *Professor of Physiology.* (1, 1922; 3, 1924)

Thompson, Randall L., S.M., Sc.D., M.D. School of Medicine, Western Reserve University, 2109 Adelbert Rd., Cleveland, O. *Assistant Professor of Bacteriology.* (6, 1937)

Thompson, William R., Ph.D. 883 Warren St., Albany, N. Y. (2, 1934)

Thomson, David Landsborough, M.A., Ph.D., F.R.S.C. McGill University, Montreal, Canada. *Professor of Biochemistry and Dean of the Faculty of Graduate Studies and Research.* (2, 1929)

Thorn, George Widmer, M.D. Peter Bent Brigham Hospital, Boston, Mass. *Professor of Medicine of Harvard University.* (1, 1939)

Tillett, William S., M.D., Sc.D. (hon.). Department of Bacteriology, New York University College of Medicine, 477 First Ave., New York City. *Professor of Medicine.* (6, 1927)

Tilt, Jennie, M.S., Ph.D. Florida State College for Women, Tallahassee. *Professor of Physiological Chemistry and Nut* 5, 1937)

Tipson, R. Stuart, Ph.D. Mellon Institute of Industrial Research, University of Pittsburgh, Pittsburgh, Pa. *Fellow, Department of Research in Pure Chemistry.* (2, 1937)

Tipton, Samuel R., Ph.D. Department of Physiology, College of Medicine, Wayne University, Detroit, Mich. *Assistant Professor in Physiology.* (1, 1940)

Tisdall, Frederick F., M.S., M.D., M.R.C.S., L.R.C.P. (London), F.R.C.P. (C.). University of Toronto, Toronto, Canada. *Associate Professor of Pediatrics; Associate Physician, Hospital for Sick Children, Department of Medicine, University of Toronto.* (2, 1922; 5, 1933)

Titus, Harry W., A.M., Ph.D. 3705 24th St., N.E., Washington 18, D. C. *Senior Biological Chemist, Bureau of Animal Industry, U. S. Department of Agriculture.* (2, 1929; 5, 1933)

Tocantins, Leandro Maués, M.D. Jefferson Medical College, Philadelphia, Pa. *Associate Professor of Medicine.* (1, 1939)

Todhunter, Elizabeth Neige, M.Sc., Ph.D., University of Alabama, University. *Associate Professor of Nutrition.* (5, 1939)

Toennies, Gerrit, Ph.D. Lankenau Hospital Research Institute, Philadelphia, Pa. *Research Chemist.* (2, 1934)

Tolle, Chester D., Ph.D. Food and Drug Administration, Federal Security Agency, Washington, D. C. *Senior Biochemist.* (5, 1942)

Tompkins, Edna H., M.D. Vanderbilt University, School of Medicine, Nashville, Tenn. *Associate Professor of Anatomy.* (4, 1941)

Torda, Clara, Ph.D., M.D.* Cornell Medical Center, New York City. *Research Fellow in Department of Medicine.* (1, 1943)

Torrey, John C., Ph.D., D.Sc. 1300 York Ave., New York City. *Professor (Emeritus) of Epidemiology, Cornell University Medical College.* (6, 1920)

Toth, Louis A., M.S., Ph.D. Tulane University School of Medicine, Station 20, New Orleans, La. *Assistant Professor of Physiology.* (1, 1940)

Tourtellotte, Dee, M.S., D.Sc. Charles B. Knox Gelatin Co., Johnstown, N. Y. (5, 1935)

Tower, Sarah Sheldon, M.D., Ph.D. Johns Hopkins Medical School, Baltimore, Md. *Associate in Anatomy.* (1, 1932)

Travell, Janet, M.D. Cornell University Medical College, New York City. *Instructor in Pharmacology.* (3, 1933)

Travis, Lee Edward, A.M., Ph.D. Dept. of Psychology, Univ. of Southern California, Los Angeles. *Major, Public Relations Officer, Army Air Force, Gardner Field, Taft, Calif.* (1, 1929)

Treffers, Henry P., Ph.D. Harvard Medical School, Boston, Mass. *Assistant Professor of Comparative Pathology and Biochemistry.* (6, 1942)

Trimble, Harry C., M.D., Ph.D. 25 Shattuck St., Boston Mass. *Assistant Professor of Biological Chemistry, Harvard Medical School.* (2, 1929; 5, 1936)

Tuft, Louis H., M.D. 1530 Locust St., Philadelphia, Pa. *Assistant Professor of Medicine, Temple University Medical School; Chief of Clinic of Allergy and Applied Immunology, Temple University Hospital.* (6, 1928)

tum Suden, Caroline, M.A., Ph.D. 80 E. Concord St., Boston, Mass. *Evans Research Fellow in Physiology, Boston University School of Medicine; Assistant, Evans Memorial Staff, Massachusetts Memorial Hospitals.* (1, 1936)

Tuohy, Edward B., M.S., M.D. Mayo Foundation, Mayo Clinic, Rochester, Minn. *Assistant Professor of Anesthesiology.* (3, 1941)

Turner, Abby H., Ph.D. Mount Holyoke College, South Hadley, Mass. *Professor of Physiology.* (1, 1928)

Turner, William A., Ph.D. Bureau of Dairy Industry, U. S. Department of Agriculture, Beltsville, Md. *Associate Chemist.* (2, 1929)

Tuttle, Waid Wright, M.A., Ph.D. University of Iowa, Iowa City. *Professor of Physiology.* (1, 1925)

Tweedy, Wilbur R., Ph.D. Loyola University School of Medicine, 706 S. Wolcott St., Chicago, Ill. *Professor and Chairman, Department of Biological Chemistry.* (2, 1931)

Tyler, David B., Ph.D.* California Institute of Technology, Pasadena. *Hixon Fund Fellow.* (1, 1943)

Unna, Klaus R. W., M.D. Merck Institute for Therapeutic Research, Rahway, N. J. *Research Associate.* (1, 1941; 5, 1942)

Upton, Morgan, M.A., Ph.D. British Purchasing Commission, 1518 K St., N.W. Washington, D. C. (1, 1934)

Urban, Frank, Ph.D. Washington University School of Medicine, St. Louis, Mo. *Assistant Professor of Biochemistry.* (2, 1932)

Vahlteich, Ella McCollum, M.A., Ph.D. 46 Hudson Ave., Edgewater, N. J. (5, 1933)

van Dyke, H. B., Ph.D., M.D. The Squibb Institute for Medical Research, New Brunswick, N. J. *Head of the Division of Pharmacology; Honorary Professor of Physiology, Rutgers University.* (1, 1925; 3, 1942)

van Harreveld, Anthonie, M.A., M.D. California Institute of Technology, Pasadena. *Associate Professor of Physiology.* (1, 1941)

Van Liere, Edward J., M.S., M.D., Ph.D. The School of Medicine, West Virginia University, Morgantown. *Professor of Physiology and Dean.* (1, 1927)

Van Slyke, Donald D., Ph.D., Sc.D., M.D. Rockefeller Institute for Medical Research, 66th St. and York Ave., New York City. *Member; Member, National Academy of Sciences.* (2, 1908)

van Wagenen, Gertrude, Ph.D. Yale University School of Medicine, New Haven, Conn. *Associate Professor.* (1, 1932)

Van Winkle, Walton, Jr., M.D. Pharmacology Division, Food and Drug Administration, Federal Security Agency, Washington, D. C. *Associate Pharmacologist.* (3, 1939)

Vars, Harry M., Ph.D. Harrison Department of Surgical Research, University of Pennsylvania Medical School, Philadelphia. *Assistant Professor of Physiological Chemistry.* (2, 1935; 5, 1935)

Venning, Eleanor H., M.S., Ph.D. University Clinic, Royal Victoria Hospital, Pine Ave., Montreal, Quebec, Canada. *Research Fellow.* (2, 1938)

Vickery, Hubert B., M.S., Ph.D. Connecticut Agricultural Experiment Station, New Haven. *Lecturer on the Chemistry of Proteins, Yale University; Biochemist in Charge, Connecticut Agricultural Experiment Station; Member, National Academy of Sciences.* (2, 1923)

Victor, Joseph, M.D. Research Division for Chronic Disease, Welfare Island, N. Y. *Experimental Pathologist, Associate in Pathology, Columbia University College of Physicians and Surgeons.* (4, 1935)

Virtue, Robert W., Ph.D. University of Denver, Denver, Colo. *Associate Professor of Chemistry.* (2, 1939)

Visscher, Maurice B., M.S., Ph.D. University of Minnesota, Minneapolis. *Professor of Physiology.* (1, 1927)

Voegtlin, Carl, Ph.D. National Cancer Institute, Bethesda, Md. *Chief; Pharmacologist Director, United States Public Health Service.* (1, 1908; 2, 1908; 3, 1908)

von Haam, Emmerich, M.D. Ohio State University, Columbus. *Professor of Pathology.* (4, 1938)

Von Oettingen, W. F., M.D., Ph.D. National Institute of Health, Division of Industrial Hygiene, Bethesda, Md. *Principal Industrial Toxicologist.* (3, 1925)

Vorwald, Arthur J., Ph.D., M.D. Lt. Commander, U.S.N.R., U. S. Naval Hospital, Annapolis, Md. (4, 1937)

Vos, Bert J., Ph.D., M.D. Food and Drug Administration, Washington, D. C. *Associate Pharmacologist.* (3, 1941)

Waddell, J. A., M.D. Monroe Hill, Medical School, University of Virginia, Charlottesville. *Professor of Pharmacology.* (3, 1916)

Waddell, James, Ph.D. E. I. duPont de Nemours & Co., New Brunswick, N. J. *Director of the Biological Laboratory.* (2, 1930; 5, 1935)

Wadsworth, Augustus B., M.D. New York State Department of Health, Albany. *Director, Division of Laboratories and Research.* (4, 1935; 6, 1920)

Waelsch, Heinrich, M.D., Ph.D. Columbia University, College of Physicians and Surgeons, 630 W. 168th St., New York City. *Research Associate in Biochemistry.* (2, 1941)

Wakeman, Alfred J., Ph.D. Hatfield Hill Road, Bethany, Conn. *Retired.* (2, 1906)

Wakerlin, George E., Ph.D., M.D. University of Illinois Medical School, 1853 W. Polk St., Chicago. *Professor of Physiology.* (1, 1933; 3, 1931)

Wakim, Khalil G., M.D., Ph.D. *University of* Indiana Medical School, Bloomington. *Professor of Physiology.* (1, 1942)

Wald, George, M.A., Ph.D. Biological Laboratories, Harvard University, Cambridge, Mass. (1, 1934)

Walker, Arthur M., M.D. University of Pennsylvania, Philadelphia. *Associate Professor of Pharmacology.* (1, 1932; 3, 1939)

Walker, Burnham S., Ph.D., M.D. Boston University School of Medicine, 80 E. Concord St., Boston, Mass. *Professor of Biochemistry.* (2, 1940)

Walker, Ernest Linwood, S.D. Second and Parnassus Aves., San Francisco, Calif. *Professor of Tropical Med., The George Williams Hooper Foundation for Medical Research, University of California.* (3, 1931)

Wallace, Edward W., Ph.D., M.D. 1203 Ryland Ave., Cincinnati, O. *Associate Professor of Pharmacology, University of Cincinnati, College of Medicine.* (3, 1938)

Wallace, George B., A.M., Sc.D. (hon.) M.D. 477 First Ave., New York City. *Professor of Pharmacology, New York University College of Medicine.* (1, 1901; 2, 1906; 3, 1909)

Wallen-Lawrence, Zonja, Ph.D. 4534 W. Pine Blvd., St. Louis 8, Mo. (2, 1937)

Walter, Carl W., M.D. Harvard Medical School, 25 Shattuck Street, Boston, Mass. *Director, Laboratory for Surgical Research; Associate in Surgery, Peter Bent Brigham Hospital.* (4, 1942)

Walters, Orville S., Ph.D., M.D. Central College, McPherson, Kan. *President.* (1, 1936)

Walton, Robert P., M.A., Ph.D., M.D. Medical College of the State of South Carolina, Charleston. *Professor of Pharmacology.* (3, 1933)

Walton, Seth T., V.M.D., M.S., Ph.D. City Health Department, Charlotte, N. C. *Director of Laboratories and Research.* (6, 1936)

Walzer, Matthew, M.D. 20 Plaza St., Brooklyn, N. Y. *Attending in Allergy, Jewish Hospital of Brooklyn.* (6, 1924)

Wang, Chi Che, M.S., Ph.D. 323 Belden Ave., Chicago, Ill. *Research Chemist, Children's Memorial Hospital; Assistant Professor, Dept. of Physiology, Northwestern University Medical College, Chicago.* (2, 1922; 5, 1933)

Wang, Shih-Chun, M.D., Ph.D.* Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York City. *Instructor in the Department of Physiology.* (1, 1943)

Wangensteen, Owen Harding, M.D. University of Minnesota, Minneapolis. *Professor of Surgery.* (4, 1931)

Warner, Emory D., M.D. Medical Laboratories Bldg., Iowa City, Ia. *Associate Professor of Pathology.* (4, 1937)

Warren, Charles O., Ph.D., M.D. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor of Physiology and Anatomy.* (1, 1941)

Warren, Madeleine Field, A.M., Ph.D. 9 High Rock St., Needham, Mass. Harvard School of Public Health, 55 Shattuck St., Boston, Mass. *Associate in Physiology.* (1, 1933)

Warren, Shields, M.D. Palmer Memorial Hospital, 195 Pilgrim Rd., Boston, Mass. *Pathologist, New England Deaconess Hospital; Assistant Professor of Pathology, Harvard Medical School.* (4, 1929)

Wartman, William Beckmann, M.D. Western Reserve University, 2085 Adelbert Rd., Cleveland, O. *Assistant Professor of Pathology.* (4, 1940)

Wasteneys, Hardolph, Ph.D., F.R.S.C. University of Toronto, Toronto, Canada. *Professor and Head of Department of Biochemistry.* (2, 1915)

Wastl, Helene, M.D. Hahnemann Medical College and Hospital, Philadelphia, Pa. *Research Associate in Pharmacology and Anatomy.* (1, 1939)

Waterman, Robert E., B.S. Research Corporation, 405 Lexington Ave., New York City. (2, 1940)

Waters, Ralph Milton, M.D. University of Wisconsin, Madison. *Professor of Anesthesia.* (3, 1937)

Watson, Cecil J., M.D., Ph.D. Department of Medicine, University Hospital, Minneapolis, Minn. *Professor and Head of Department of Medicine.* (4, 1941)

Watson, John B., A.M., Ph.D., LL.D. 420 Lexington Ave., New York City. *Vice President of the J. Walter Thompson Co.* (1, 1907)

Waud, Russell A., M.D., M.Sc., Ph.D. Medical School, University of Western Ontario, London, Canada. *Professor of Pharmacology.* (1, 1925; 3, 1931)

Waugh, David F., Ph.D.* Department of Biology and Biological Engineering, Massachusetts Institute of Technology, Cambridge. *Assistant Professor of Physical Biology.* (1, 1943)

Wearn, Joseph T., M.D. Lakeside Hospital, Cleveland, O. *Professor of Medicine, Western Reserve University; Director of Medicine, Lakeside Hospital.* (1, 1921)

Weatherby, J. H., M.A., Ph.D. Medical College of Virginia, Richmond. *Research Associate in Pharmacology.* (3, 1941)

Weber, Clarence J., M.D., Ph.D. University of Kansas Hospitals, Kansas City. *Assistant Professor of Research Medicine.* (2, 1931)

Webster, Bruce, M.D., C.M. Cornell University Medical College, 1300 York Ave., New York City. *Assistant Professor Medicine; Associate Attending Physician, New York Hospital.* (5 1935)

Weed, Lewis H., A.M., M.D., Sc.D. Johns Hopkins University Medical School, Baltimore, Md. *Professor of Anatomy.* (1, 1919)

Wégria, René, M.D. Department of Medicine, Presbyterian Hospital, 622 W. 168th St., New York City. (1, 1941)

Weichert, Charles K., Ph.D. University of Cincinnati, Cincinnati, O. *Assistant Professor of Zoology.* (1, 1935)

Weil, Alfred J., M.D. Lederle Laboratories, Inc., Pearl River, N. Y. *Immunologist.* (6, 1940)

Weil, Arthur, M.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Associate Professor of Neuropathology.* (4, 1940)

Weil, Leopold, Ph.D. Eastern Regional Research Laboratory, U. S. Department of Agriculture, Chestnut Hill Station, Philadelphia, Pa. *Associate Chemist.* (2, 1942)

Weir, Everett G., M.S., Ph.D. School of Medicine, Howard University, Washington, D. C. *Assistant Professor of Physiology.* (1, 1941)

Weiss, Charles, M.S., Ph.D., M.D. Mount Zion Hospital, San Francisco, Calif. *Associate Professor of Research Medicine and Lecturer in Pediatrics, University of California; Director of Clinical and Research Laboratories, Mount Zion Hospital.* (4, 1934; 6, 1920)

Weiss, Emil, M.D., Ph.D. 2318 Irving Park Rd., Chicago, Ill. *Pathologist, Chicago Eye, Ear, Nose and Throat Hospital.* (6, 1927)

Weiss, Paul, Ph.D. University of Chicago, Chicago, Ill. *Professor of Zoology.* (1, 1936)

Welch, Arnold DeMerritt, Ph.D., M.D. Medical Research Division, Sharp and Dohme, Inc., Glenolden, Pa. *Director of Research.* (3, 1942)

Welch, Henry. Ph.D. Bacteriological Section, U. S. Food and Drug Administration, Washington, D. C. *Senior Bacteriologist.* (6, 1932)

Weld, Charles Beecher, M.A., M.D. Dalhousie University, Halifax, N.S., Canada. *Professor of Physiology.* (1, 1936)

Weld, Mrs. Julia T. College of Physicians and Surgeons, 630 W. 168th St., New York City. *Research Associate in Pathology.* (6, 1920)

Welker, William H., A.C., Ph.D., D.Sc. 1853 W. Polk St., Chicago, Ill. *Professor of Physiological Chemistry and Head of the Department, College of Medicine, University of Illinois.* (2, 1906)

Weller, Carl Vernon, M.D. 1130 Fair Oaks Parkway, Ann Arbor, Mich. *Professor of Pathology and Chairman; Department of Pathology, University of Michigan.* (4, 1923)

Wells, Herbert S., M.D. Bowman Gray School of Medicine, Winston-Salem, N. C. *Professor of Physiology and Pharmacology.* (1, 1932)

Wendel, William B., Ph.D. College of Medicine, University of Tennessee, Memphis. *Associate Professor of Chemistry.* (2, 1932)

Werkman, C. H., Ph.D. Science Hall, Iowa State College, Ames. *Professor in Charge, Bacteriology Section.* (2, 1942)

Werle, Jacob M., M.D.* 4478 Broadale Ave., Cleveland, O. *1st Lieutenant, Medical Corps, School of Aviation Medicine, Randolph Field, San Antonio, Texas.* (1, 1943)

Werner, Harold W., Ph.D. Division of Industrial Hygiene and Toxicology, National Institute of Health, Bethesda, Md. *Pharmacologist.* (3, 1942)

Wertenberger, Grace E., S.M., Ph.D.* Women's Medical College of Pennsylvania, Philadelphia. *Assistant Professor of Physiology.* (1, 1943)

Wesson, Laurence Goddard, Ph.D. Forsyth Dental Infirmary, Boston, Mass. *Research Biochemist.* (2, 1929; 3, 1932)

West, Edward S., M.S., Ph.D. University of Oregon Medical School, Portland. *Professor of Biochemistry.* (2, 1925)

West, Randolph, M.A., M.D. 622 W. 168th St., New York City. *Associate Professor of Medicine, Columbia University.* (2, 1931)

Weymouth, Frank W., Ph.D. Stanford University, Calif. *Professor of Physiology and Executive of the Department.* (1, 1917)

Wheeler, George W., M.D. New York Hospital, 525 E. 68th St., New York City. *Superintendent.* (6, 1920)

Wheeler, Kenneth M., Ph.D. Bureau of Laboratories, Connecticut State Department of Health, 1179 Main St., Hartford. *Research Microbiologist.* (6, 1938)

Wheeler, Mary W., M.A. Division of Laboratories and Research, New York State Department of Health, Albany. *Associate Bacteriologist.* (6, 1933)

Wheeler, Ruth, Ph.D. Vassar College, Poughkeepsie, N. Y. *Professor of Physiology and Nutrition.* (2, 1915; 5, 1933)

Wheelon, Homer, M.S., M.D. American Bank Bldg., Seattle, Wash. (1, 1919)

Whipple, George H., M.D., Sc.D. University of Rochester, Rochester, N. Y. *Professor of Pathology and Dean of the School of Medicine and Dentistry; Member of the National Academy of Sciences.* (1, 1911; 4, prior to 1920)

White, Abraham, M.A., Ph.D. 333 Cedar St., New Haven, Conn. *Associate Professor of Physiological Chemistry, Medical School, Yale University.* (2, 1934; 5, 1937)

White, Frank D., Ph.D., F.I.C. Medical College, University of Manitoba, Winnipeg, Canada. *Assistant Professor of Biochemistry, Faculty of Medicine.* (2, 1931)

White, Harvey Lester, M.D. Station Hospital, A.P.O. 726, Seattle, Wash. *Colonel, M.C.; Associate Professor of Physiology, Washington University Medical School, St. Louis, Mo.* (1, 1923)

White, Julius, A.M., Ph.D. Station Hospital, Camp Gordon Johnston, Florida. *Captain, U. S. Army.* (2, 1937)

White, Paul Dudley, M.D., Massachusetts General Hospital, Boston. *Lecturer in Medicine, Harvard Medical School; Physician (in charge of Cardiac Clinics and Laboratory), Mass. General Hospital.* (3, 1921)

Whitehead, Richard W., M.A., M.D. University of Colorado School of Medicine, 4200 E. Ninth Ave., Denver. *Professor of Physiology and Pharmacology.* (1, 1933; 3, 1928)

Wiener, Alexander S., M.D. 64 Rutland Rd., Brooklyn, N. Y. *Bacteriologist and Serologist to Office of Chief Medical Examiner of New York City; Head of Transfusion Division, Jewish Hospital of Brooklyn.* (6, 1932)

Wiersma, Cornelis A. G., M.A., Ph.D. California Institute of Technology, Pasadena. *Associate Professor of Physiology.* (1, 1941)

Wiggers, Carl J., M.D., Sc.D. Medical School, Western Reserve University, Cleveland, O. *Professor and Director of Physiology.* (1, 1907; 3, 1909)

Wiggers, Harold C., Ph.D. College of Medicine, University of Illinois, 1853 W. Polk St., Chicago. *Associate Professor of Physiology.* (1, 1938)

Wigodsky, Herman S., Ph.D., M.D.* Research Division, Air Surgeon's Office, Hdqtrs. Army Air Forces, War D

D. C. *Major, M.C.; Chief, Physiological Branch.* (1, 1943)

Wilder, Russell M., Ph.D., M.D. Mayo Clinic, Rochester, Minn. *Professor of Medicine, Mayo Foundation, University of Minnesota.* (1, 1921; 4, 1924; 5, 1933)

Wiley, Frank H., M.S., Ph.D. Food and Drug Administration, Federal Security Agency, Washington 25, D. C. *Senior Chemist.* (2, 1933)

Wilhelmi, Alfred E., Ph.D. 333 Cedar St., New Haven, Conn. Yale University School of Medicine. *Instructor in Physiological Chemistry.* (2, 1942)

Wilhelmj, Charles Martel, M.D. Creighton University School of Medicine, Omaha, Neb. *Professor of Physiology.* (1, 1931)

Wilkerson, Vernon A., M.D., Ph.D. Howard University Medical School, Washington, D. C. *Professor and Head of Department of Biochemistry.* (2, 1936)

Williams, Harold H., Ph.D. 660 Frederick St., Detroit, Mich. *Associate Director, Research Laboratory, Children's Fund of Michigan.* (2, 1938; 5, 1936)

Williams, Horatio B., M.D., Sc.D. 632 W. 168th St., New York City. *Dalton Professor of Physiology Emeritus, Columbia University.* (1, 1912)

Williams, Ray D., M.D. 6834 Waterman St., St. Louis, Mo. *Research Fellow.* (5, 1941)

Williams, Robert R., D.Sc. Bell Telephone Laboratories, 297 Summit Ave., Summit, N. J. *Chemical Director.* (5, 1941)

Williams, Robert Hardin, M.D. Thorndike Laboratory, Boston City Hospital, Boston, Mass. *Instructor in Medicine, Harvard Medical School; Assistant Physician, Thorndike Memorial Laboratory; Junior Visiting Physician, II and IV Medical Services (Harvard) Boston City Hospital.* (4, 1940)

Williams, Robert R., M.S., D.Sc. 297 Summit Ave., Summit, N. J. *Chemical Director, Bell Telephone Laboratories.* (2, 1919)

Williams, Roger J., Ph.D., D.Sc. University of Texas, Department of Chemistry, Austin. *Professor of Chemistry.* (2, 1931)

Wills, J. H., M.S., Ph.D.* University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. *Associate in Pharmacology.* (1, 1943)

Wilson, David Wright, M.S., Ph.D. University of Pennsylvania Medical School, Philadelphia. *Professor of Physiological Chemistry.* (1, 1915; 2, 1915)

Wilson, Frank N., M.D. University Hospital, Ann Arbor, Mich. *Professor of Medicine, University of Michigan.* (4, 1925)

Wilson, Karl M., M.D. University of Rochester, School of Medicine, Rochester, N. Y. *Professor of Obstetrics and Gynecology.* (4, 1927)

Wilson, P. W., Ph.D. Department of Agricultural Bacteriology, University of Wisconsin, Madison. *Associate Professor in Agricultural Bacteriology.* (2, 1939)

Wilson, Robert H., Ph.D. U. S. Department of Agriculture, Stanford University School of Medicine, San Francisco, Calif. *Pharmacologist.* (3, 1937)

Winder, Claude V., Sc.D. 1927 Dexter Ave., Ann Arbor, Mich. *Pharmacologist, Parke, Davis & Company, Detroit, Mich.* (1, 1938)

Windle, William Frederick, Ph.D. Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. *Professor of Anatomy.* (1, 1937)

Winkenwerder, Walter LaF., M.D. Brooklandville, Md. *Associate in Medicine, Johns Hopkins Medical School.* (6, 1938)

Winkler, Alexander Woodward, A.M., M.D. New Haven Hospital, 789 Howard Ave., New Haven, Conn. *Assistant Professor of Medicine, Yale University School of Medicine.* (1, 1940)

Winter, Charles A., Ph.D. State University of Iowa, College of Medicine, Iowa City. *Assistant Professor of Physiology.* (1, 1940)

Winter, Irwin Clinton, Ph.D., M.D. University of Oklahoma School of Medicine, Oklahoma City. *Associate Professor in Pharmacology.* (3, 1941)

Winters, Jet C., M.A., Ph.D. University of Texas, Austin. *Professor of Home Economics.* (5, 1933)

Winternitz, M. C., M.D. Yale University School of Medicine, New Haven, Conn. *Anthony N. Brady Professor of Pathology.* (4, prior to 1920)

Wintersteiner, Oskar, Ph.D. The Squibb Institute for Medical Research, New Brunswick, N. J. *Head, Division of Organic Chemistry; Honorary Professor of Biochemistry, Rutgers University.* (2, 1930)

Wintrobe, Maxwell Myer, M.D., Ph.D. University of Utah School of Medicine, Salt Lake City. *Head and Professor of the Department of Internal Medicine.* (4, 1940)

Wiseman, Bruce Kenneth, M.D. Kinsman Hall, Ohio State University, Columbus. *Professor of Medicine; Assistant Director of Medical Research.* (4, 1932)

Wislocki, George B., M.D. Harvard University Medical School, 25 Shattuck St., Boston, Mass. *Parkman Professor of Anatomy.* (1, 1924)

Witebsky, Ernest, M.D. Buffalo General Hospital, 100 High St., Buffalo, N. Y. *Professor of Bacteriology and Immunology.* (6, 1935)

Witzemann, Edgar J., M.A., Ph.D. Service Memorial Building, University of Wisconsin, Madison. *Associate Professor of Physiological Chemistry.* (2, 1925)

Wolbach, S. Burt, M.D. Harvard University Medical School, 25 Shattuck St., Boston, Mass. *Shattuck Professor of Pathological Anatomy;*

Member, National Academy of Sciences. (4, prior to 1920)

Wolff, Harold G., M.D., M.A. New York Hospital, 525 E. 68th St., New York City. *Associate Professor of Medicine, Cornell University Medical College; Associate Attending Physician, New York Hospital.* (1, 1930; 3, 1942)

Wood, Earl H., M.S., Ph.D., M.D.* Mayo Aeromedical Unit, Mayo Foundation, Rochester, Minn. *Assistant in Physiology.* (1, 1943)

Wood, Horatio C., Jr., M.D., Ph.M. 319 S. 41st St., Philadelphia, Pa. *Professor of Pharmacology and Therapeutics, University of Pennsylvania; Professor of Materia Medica, Philadelphia College of Pharmacy and Science.* (3, 1908)

Woodbury, Robert A., Ph.D., M.D. University of Georgia, School of Medicine, Augusta. *Professor of Pharmacology.* (1, 1936; 3, 1941)

Woodruff, Lorande Loss, A.M., Ph.D. Yale University, New Haven, Conn. *Professor of Protozoology; Member, National Academy of Sciences.* (1, 1910)

Woods, Alan C., M.D. Wilmer Institute, Johns Hopkins Hospital, Baltimore, Md. *Ophthalmologist-in-Chief; Acting Professor of Ophthalmology, Johns Hopkins University; Director, Wilmer Ophthalmological Institute.* (6, 1918)

Woods, Ella, A.M., Ph.D. University of Idaho, Moscow. *Home Economist, Experiment Station.* (2, 1925; 5, 1933)

Woodward, Alvalyn E., M.S., Ph.D. University of Michigan, Ann Arbor. *Assistant Professor of Zoology.* (1, 1932)

Woodyatt, Rollin T., M.D. 237 E. Delaware Place, Chicago, Ill. *Professor of Medicine, Rush Medical College, University of Chicago.* (2, 1912)

Woolley, Dillworth W., Ph.D. Rockefeller Institute for Medical Research, 66th St., and York Ave., New York City. *Fellow.* (5, 1941)

Woolsey, Clinton N., M.D. Johns Hopkins University School of Medicine, Baltimore, Md. *Fellow in Orthopedic Surgery.* (1, 1938)

Wright, Angus, M.D. University of Southern California Medical School, 657 S. Westlake Ave., Los Angeles. *Instructor in Pathology; Pathologist, California Hospital.* (4, 1935)

Wright, Arthur W., M.D. Albany Medical College, New Scotland Ave., Albany, N. Y. *Professor of Pathology and Bacteriology.* (4, 1941)

Wright, Charles Ingham, M.S., Ph.D. National Institute of Health, Bethesda, Md. *Pharmacologist, U. S. Public Health Service.* (1, 1935; 3, 1936)

Wright, Harold N., M.S., Ph[illegible]ersity of Minnesota, Minneapolis. *A[illegible]ofessor of Pharmacology.* (3, 1933)

Wright, Sydney L., M.A., Ph.D. Endsmeet Farm Glenside, Pa. (2, 1933)

Wulzen, Rosalind, M.S., Ph.D. Oregon State College, Corvallis. *Assistant Professor of Zoology.* (1, 1916)

Wyckoff, Ralph W. G., Ph.D. Reichel Laboratories, Kimberton, Pa. *Technical Director.* (6, 1940)

Wyman, Jeffries, Jr., Ph.D. Harvard University, Cambridge, Mass. *Associate Professor of Zoology and Chairman of the Board of Tutors in Division of Biology.* (1, 1928)

Wyman, Leland C., Ph.D. Boston University School of Medicine, Boston, Mass. *Associate Professor of Physiology.* (1, 1927)

Wynne, Arthur M., M.A., Ph.D., F.R.S.C. Department of Biochemistry, University of Toronto, Toronto, Canada. *Professor of Biochemistry.* (2, 1940)

Yerkes, Robert M., Ph.D. Yale Laboratories of Primate Biology, 333 Cedar St., New Haven, Conn. *Professor of Psychobiology, Yale University; Member of the National Academy of Sciences.* (1, 1901)

Yonkman, Frederick F., Ph.D., M.D. Wayne University College of Medicine, Detroit, Mich. *Professor of Pharmacology and Therapeutics.* (3, 1931)

Youmans, William Barton, M.A., Ph.D. University of Oregon Medical School, Portland. *Assoc. Professor of Physiology.* (1, 1939)

Young, A. G., Ph.D., M.D. 520 Commonwealth Ave., Boston, Mass. *Assistant Professor of Therapeutics, Boston University School of Medicine; Medical Director, Corey Hill Hospital, Brookline.* (3, 1925)

Young, E. G., Ph.D., F.R.S.C. Dalhousie University, Halifax, N. S., Canada. *Professor of Biochemistry.* (2, 1925)

Youngburg, Guy E., M.S., Ph.D. 179 Admiral Rd., Buffalo 16, N. Y. *Professor of Biological Chemistry, University of Buffalo.* (2, 1927)

Yuile, Charles L., M.D., C.M. Pathological Institute, McGill University, Montreal, Canada. *Assistant Professor of Pathology.* (4, 1941)

Zechmeister, L. California Institute of Technology, Pasadena. *Professor of Organic Chemistry.* (2, 1941)

Zeckwer, Isolde T., M.D. School of Medicine, University of Pennsylvania, Philadelphia. *Assistant Professor of Pathology.* (1, 1934; 4, 1927)

Zimmerman, Harry M., M.D. Yale University School of Medicine, 310 Cedar St., New Haven, Conn. *Associate Professor of Patholog[illegible]* 1933)

Zwemer, Raymund L., Ph.D. C[illegible]cians and Surgeons, Columb[illegible] W. 168th St., New York *[illegible]fessor of Anatomy.*

SUMMARY OF MEMBERSHIP

The American Physiological Society	842
The American Society of Biological Chemists	608
The American Society for Pharmacology and Experimental Therapeutics	284
The American Society for Experimental Pathology	295
The American Institute of Nutrition	271
American Association of Immunologists	246
Total Members by Societies	2546

DECEASED MEMBERS

Abel, John J. (1, 2, 3) May 26, 1938.
Abbott, A. C. (1) September 11, 1936.
Abramson, H. L. (6) April, 1934.
Adami, J. George (2) August 29, 1926.
Adler, Herman M. (2) December 6, 1935.
Adler, Isaac (3) February 2, 1912.
Alsberg, Carl L. (1, 2) October 31, 1940.
Apfelbach, Carl Wesley (4) June 25, 1943.
Armsby, H. P. (1) October 19, 1921.
Atkinson, Harry V. (3) May 7, 1939.
Atwater, W. O. (1) September 22, 1907.
Austin, William C. (2) November 20, 1935.
Bancroft, F. W. (1) August 23, 1924.
Banting, F. G. (3) February 21, 1941.
Banzhaf, Edwin J. (2, 6) March 17, 1931.
Barbour, Henry Gray (1, 2, 3) September 23, 1943.
Benedict, Stanley R. (1, 2) December 21, 1936.
Beyer, Henry G. (1) December 9, 1918.
Black, Otis Fisher (2) October 14, 1933.
Blackfan, Kenneth D. (5) November 5, 1941.
Bleile, Albert M. (1) August 16, 1933.
Bodansky, Meyer (2) June 14, 1941.
Bowditch, Henry P. (1) March 13, 1911.
Braman, Winfred W. (5) March 24, 1937.
Brodie, Maurice (6) May 9, 1939.
Brodie, Thomas G. (1, 2) August 20, 1916.
Brown, Wade H. (3, 4) August 4, 1942.
Brubaker, Albert P. (1) April 29, 1943.
Bull, Carroll G. (6) May 30, 1931.
Bullowa, Jesse G. M. (3, 6) November 9, 1943
Burget, G. E. (1) June 4, 1938.
Busch, Fred C. (1) January 3, 1914.
Callison, William E. (3) February 26, 1937.
Chapman, Henry C. (1) September 7, 1909.
Chillingworth, F. P. (1) June 30, 1938.
Clark, Admont Halsey (1) October 13, 1918.
Clark, G. P. (1) September 1, 1907.
Cleghorn, Allen M. (1) March 20, 1916.
Cohen, Seymour J. (3) June 11, 1942.
Connor, Charles L. (4) June 12, 1941.
Cook, Frank C. (2) June 19, 1923.
Coulter, Calvin B. (4) May 10, 1940.
Crawford, Albert C. (3) March 14, 1921.
Crile, George W. (1, 3) January 7, 1943.
Cullen, Glenn E. (2, 5) April 11, 1940.
Curtis, John G. (1) September 20, 1913.
Cushing, Harvey (1, 4) October 7, 1939.
Cushny, A. R. (1) February 25, 1926.
Dalton, J. C. (1) February 12, 1889.
Dastré, A. (1h) October 25, 1917.
D'Aunoy, Joseph Rigney (4) September 17, 1941
Davis, Alice Rohde (2) August 22, 1933.
Dawson, Wilfred T. (1, 3) September 19, 1939.
Denis, Willey (1, 3) January 9, 1929.
Donaldson, Henry H. (1) January 24, 1938.
Dooley, David H. (1) April 11, 1927.
Dreyer, George P. (1) February 27, 1931.
Dunham, Edward K. (2) April 16, 1922.
Dusser de Barenne, J. G. (1, 3) June 9, 1940.
Edmunds, Charles W. (1, 3) March 1, 1941.
Englemann, Th. W. (1h) May 20, 1909.
Ets, Harold N. (1, 3) June 25, 1943.
Ewing, Ephraim MacDonald (1) August 27, 1925.
Fitch, Richard H. (1, 3) January 7, 1939.
Fitz, George W. (1) October 28, 1934.
Folin, Otto (1, 2, 3) October 26, 1934.
Foster, Nellis Barnes (2) August 20, 1933.
Franz, Shepherd Ivory (1) October 14, 1933.
Gager, C. Stuart (2) August 9, 1943.
Gates, Frederick L. (3, 4) June 17, 1933.
Gay, Frederick P. (4, 6) July 14, 1939.
Goodale, George L. (1) April 12, 1923.
Gortner, Ross A. (2) September 30, 1942.
Greeley, A. W. (1) May 15, 1904.
Gross, Louis (4) October 17, 1937.
Hall, G. Stanley (1) April 24, 1924.
Halsted, William S. (4) September 7, 1922.
Hammersten, O. (1h) September 21, 1932.
Harding, Victor John (2) July 10, 1934.
Hare, Hobart Amory (1) June 15, 1931.
Haskins, Howard Davis (1, 2) November 19, 1933.
Hawkins, James A., (1, 2) July 26, 1937.
Henderson, Lawrence J. (1, 2) February 10, 1942.
Herter, C. H. (1) December 5, 1910.
Hess, Alfred Fabian (2, 5) December 5, 1933.
Hewlett, Albion Walter (1, 3, 4) November 10, 1925.
Hirschfelder, Arthur D. (1, 2, 3) October 11, 1942.
Hiss, Philip H., Jr. (2, 3) February 27, 1913.
Hofmeister, F. (1h) July 26, 1922
Hooper, Charles Warren (1) January 27, 1936.
Hough, Theodore (1) November 30, 1924.
Howland, John (2) June 20, 1926.
Huber, G. Carl (1) December 26, 1934.
Inman, Ondess L. (2) July 21, 1942.
Jackson, Holmes C. (1, 2) October 25, 1927.

Jaffe, Hermann R. (4, 6) December 17, 1937.
James, Wm. (1) August 26, 1910.
Jenkins, Oliver P. (1) January 9, 1935.
Jones, Frederic S. (4) October 19, 1931.
Jones, Walter (1, 2) February 28, 1935.
Jordan, Edwin O. (1) September 2, 1936.
Joseph, Don R. (1, 3) July 9, 1928.
Kahn, Max (2) April 8, 1926.
Kastle, Joseph H. (1, 2) September 21, 1916.
King, Walter E. (6) May 1, 1936.
Klotz, Oskar (4) November 3, 1936.
Koch, Waldemar (3) February 2, 1912.
Koessler, Karl K. (2, 4, 6) February 13, 1928.
Krause, Allen K. (4) May 12, 1941.
Kriss, Max (5) November 15, 1941.
Krumwiede, Charles (6) December 29, 1930.
Landsteiner, Karl (4, 6) June 26, 1943.
Langley, J. N. (1) November 5, 1925.
Langworthy, Charles F. (2) March 3, 1932.
Lee, Frederic S. (1) December 14, 1939.
Leech, Paul Nicholas (3) January 14, 1941.
Levene, Phoebus A. (1, 2) September 6, 1940.
Lewis, Dean (1) October 9, 1941.
Lewis, Paul A. (3, 4, 6) June 30, 1929.
Lingle, D. J. (1) November 27, 1936.
Loeb, Jacques (1, 2) February 11, 1924.
Loerenhart, A. S. (1, 2, 3) April 20, 1929.
Long, John H. (2) June 14, 1918.
Lombard, Warren P. (1) July 13, 1939.
Lusk, Graham (1, 2, 5) July 18, 1932.
Lyon, Elias P. (1) May 4, 1937.
Macallum, Archibald Byron (1, 2) April 5, 1934.
Macleod, John James Rickard (1) March 16, 1935.
McCordock, Howard A. (4) November 13, 1938.
McGlone, Bartgis (1) November 10, 1941.
McKinley, Earl B. (4, 6) July 28, 1938.
Magnus, Rudolf (3) July 25, 1927.
Mall, Franklin P. (1) November 17, 1917.
Mallory, F. B. (4) September 28, 1941.
Mandel, John A. (1, 2) May 5, 1929.
Mann, Gustav (1) July 18, 1921.
Marriott, W. McKim (2, 5) November 11, 1936.
Marshall, John (1, 2) January 5, 1925.
Martin, Ernest Gale (1) October 17, 1934.
Martin, H. Newell (1) October 27, 1896.
Matson, Ray W. (6) September, 1934.
Mathews, Samuel A. (1, 3) February 19, 1928.
Maximow, Alexander A. (4) December 4, 1928.
Maxwell, S. S. (1) January 28, 1939.
Meigs, Edward B. (1, 2, 5) November 5, 1940.
Mellus, E. Linden (1) December 17, 1923.
Meltzer, S. J. (1, 2, 3, 4) November 7, 1920.
Mendel, Lafayette B. (1, 2, 3, 5) December 9, 1935.
Meyer, Hans H. (3h) October 6, 1939.
Miller, Elmer S. (2) June 11, 1941.
Miller, Joseph L. (1, 3) August 6, 1937.
Mills, Thomas W. (1) February 13, 1915.
Minot, Charles S. (1) November 19, 1914.
Mitchell, S. Weir (1) January 4, 1914.
Moore, Lillian Mary (1) August 1, 1929.
Morris, J. Lucien (2) March 19, 1926.
Moyer, Laurence S. (2) June 8, 1942.
Myers, Harold B. (3) March 16, 1937.
Neuhausen, Benj. S. (2) August 20, 1923.
Nelson, Louis (3) April 14, 1912.
Nichols, Henry J. (4) September 2, 1927.
Noguchi, Hideyo (4, 6) May 21, 1928.
Osborne, Thomas Burr (1, 2) January 29, 1929.
Osler, Sir William (1) December 29, 1919.
Ott, Isaac (1, 3) January 1, 1916.
Park, William H. (4, 6h) April 6, 1939.
Pavlov, Ivan P. (1h) February 27, 1936.
Pearce, Richard M., Jr. (4) February 16, 1930.
Perla, David (4, 6) June 14, 1940.
Peters, H. C. (1) July 13, 1912.
Pettibone, C. J. V. (2) March 8, 1929.
Pfaff, Franz (1, 2) September 26, 1926.
Pflüger, E. (1h) March 17, 1910.
Pincussen, Ludwig (2) November 30, 1941.
Plant, Oscar H. (1, 3) October 1, 1939.
Prince, Alexander L. (1) May 25, 1938.
Ranson, S. W. (1) August 30, 1942.
Reichert, Edward T. (1) December 25, 1931.
Richards, Herbert M. (2) January 9, 1928.
Robertson, T. Brailsford (2) January 27, 1930.
Rockwood, Elbert W. (2) July 17, 1935.
Rosenbloom, Jacob (2) September 25, 1923.
Rose, Mary Schwartz (1, 2, 5) February 1, 1941.
Ross, Ellison, L. (2, 3) December 21, 1938.
Rowe, Allan Winter (1, 2, 5) December 6, 1934.
Rutan, Robert F. (2) February 19, 1930.
Schafer, Sir Edward Sharpey (1h) March 29, 1935.
Schiff, Fritz (6) 1940.
Schoenheimer, Rudolf (2) September 11, 1941.
Scott, J. M. Duncan (1) January 28, 1930.
Sedgwick, William T. (1) January 26, 1921.
Sellards, Andrew Watson (4) December 1, 1942.
Sewall, Henry (1) July 8, 1936.
Shaw, Louis A. (1) August 27, 1940.
Sheldon, Ralph E. (1) July 9, 1918.
Shorey, Edmund C. (2) January 30, 1939.
Simon, Charles E. (1, 2) November 8, 1927.
Sinclair, A. N. (6) October 21, 1930.
Simpson, G. E. (2) December 23, 1927.
Simpson, Sutherland (1) March 2, 1926.
Smith, H. E. (1) October 9, 1933.
Smith, R. Meade (1) 1919.
Smith, Theobald (4h, 6) December 10, 1934.
Spaeth, Reynold A. (1) January 26, 1925.
Sternberg, G. M. (1) November 3, 1915.
Stevens, Herman C. (1) May 27, 1934.
Stewart, G. N. (1, 3, 4) May 28, 1931.
Stiles, Percy G. (1) July 5, 1936.
Storey, Thomas A. (1) October 27, 1943.
Straus, Henry W. (6) 1937.
Terry, Oliver P. (1) December 6, 1933.
Thatcher, Roscoe Wilfred (2) December 6, 1933.
Thompson, Wm. G. (1) October 27, 1927.

Trask, James D. (6).May 24, 1942.
Underhill, Frank P. (1, 2, 3) June 28, 1932.
Van Slyke, Lucius L. (2) September 30, 1931.
Vaughan, Victor C. (1, 4) October 21, 1929.
Vincent, S. (1) December 31, 1933.
Von Brücke, Ernest T. (1) June 12, 1941.
von Voit, C. (1h) January 31, 1908.
Walton, D. C. (3) March 6, 1942.
Warren, Joseph W. (1) December 20, 1916.
Warthin, Aldred Scott (4) May 23, 1931.
Webster, Leslie T. (4) July 12, 1943.
Webster, Ralph W. (2) July 2, 1930.
Weil, Richard (3, 6) November 19, 1917.
Weiss, Soma (3) January 31, 1942.
Welch, William H. (1, 4h) April 30, 1934.
Wells, H. Gideon (2, 4, 6) April 26, 1943.
Westbrook, Frank F. (1) October 21, 1918.
Wherry, William Buchanan (4) November 1, 1936.
Wiley, Harvey W. (2) June 30, 1930.
Woelfel, A. (1) January 31, 1920.
Wood, Horatio C. (1) January 3, 1920.
Zinsser, Hans (4, 6) September 4, 1940.

INDEX